EXAMINATION OF MICRONUTRIENTS FOR CHILDREN: THEIR COMPOSITION, THE ROLE THEY PLAY IN PSYCHOLOGICAL WELL-BEING AND PARENTS MOTIVATIONS FOR PURCHASING

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Amy Harris

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Abstract

Background: Micronutrient supplements are a formulae comprised of essential nutrients including: vitamins, minerals and amino acids.

Objective: This study investigates the composition of micronutrient supplements and the differences found between micronutrient supplements used in child focused research and supplements available over the counter. This study also aims to explore the reasons for which New Zealand parents give their children micronutrient supplements.

Methods: These areas are explored in two separate investigations. The first study begins by identifying the psychologically based micronutrient literature, then brakes down the vitamin ingredient composition of the micronutrient supplements that are found to significantly improve behaviour or cognition in children. These findings are compared to the composition of over the counter commercial micronutrient supplements. The second study had 365 participants and was carried out in the form of a web-based survey.

Results: A number of studies were found that showed significant behavioural or cognitive improvements in children as a result of micronutrient supplementation. The median vitamin daily doses from the effective supplements were found to be greater than the daily doses found in the over the counter products. This difference was found to be significant for most of the B vitamins: B_1 ($p < .05$), B_3 ($p < .05$), B_5 ($p < .001$), B_6 ($p < .05$), B7 ($p < .05$), B9 ($p = .001$), B12 ($p < .05$). The difference was also found to be significant for vitamin C ($p < .05$) and vitamin D ($p < .05$). The difference between the research and commercial supplement median doses was not found to be significant for vitamin A ($p < .3$) or vitamin B2 ($p < .2$). The web-based survey revealed that New Zealand parent's do not in general, give their children micronutrient supplements for psychologically based reasons. The most common motivation for giving their child a micronutrient supplement was found to be for the prevention of colds and illnesses.

Conclusions: Micronutrient supplements that are effective in research with a child based psychological focus have in general significantly greater vitamin dosages than commercially available supplements. This indicates that the results found in scientific micronutrient studies may not be generalisable to over the counter supplements. Comparing the ingredients and dosages in micronutrient supplements is however, a complex process and further investigation is required. Furthermore, this research showed that micronutrient supplements appear to be given to New Zealand children for purposes that are not psychologically based, but are based more on physical health.

Introduction

1. Micronutrients Introduction

Over the last decade interest has slowly developed in the use of micronutrients to influence psychological functions. To date, micronutrient research has been varied across the psychological areas of mood, behaviour and cognition. The repeated finding of successful amelioration of psychological functions has greatly increased the use of micronutrients in the approach to treating psychiatric disorders. The rationale behind focusing on multi-ingredient micronutrient supplement is based on the premise that the mechanism of action of micronutrients might involve additive or synergistic effects of complex mixtures. Humans evolved to require a mixture of nutrients, hence dietary interventions of single ingredients may risk upsetting the balance of nutrients and creating deficiencies in other nutrients (Mertz, 1994). Therefore, a natural intervention approach to evaluate might be a broad array of well-balanced micronutrients, and the administration of these nutrients together provides an excellent opportunity to examine how nutrients may work in combination.

Micronutrients are substances required in small amounts examples include vitamins, minerals and some amino acids, they are crucial for normal and healthy bodily function (Institute of Medicine, 2001). This is in contrast to macronutrients which are required in larger amounts; for example, some proteins, fats and carbohydrates (Institute of Medicine, 2001). The absence of a vitamin blocks one or more specific metabolic reactions in a cell and eventually may disrupt the metabolic balance within a cell and in our entire body, making their role an essential one (MacWilliam, 2009). For the purposes of this study a micronutrient supplement was defined as a supplement containing three or more vitamins and/or minerals and/or amino acids, and named the supplement a multi nutrient, or multi vitamin and/or mineral, or a micronutrient supplement.

Micronutrient supplements are regulated in NZ law under the Dietary Supplements Regulations (1985), which was amended in 2010. A substance is a dietary supplement based on its ingredients, its purpose and the manner in which it is presented to the market (Dietary Supplements Regulations, 1985). The product must be taken orally in a 'therapeutic type' dose form, and abide by the recommended daily intakes on a number of vitamin and

mineral daily dosages. The maximum daily dosage regulations in New Zealand for products designed for children adopted from the US Food and Nutrition Board of the National Academy of Science. The NZ regulations have no specific restrictions on the psychological claims supplements can imply. A number of commercial micronutrient manufacturers make advisories that they promote an aspect of mental or emotional well-being and yet there is no requirement for provision of evidence to support such advisories.

The supplements used in child-focused micronutrient studies are not those found in supermarkets, pharmacies or health-food stores, but are high end products available solely on-line direct from the producing company, or were created specifically for research purposes. It was not clear prior to this investigation whether the supplements used in studies have comparable compositions to those sold over the counter. This study aims to identify a broad range of micronutrient products for children that are available over the counter, and compare them in both ingredients and dosages to supplements used in research studies that produce significant behavioural symptoms reduction or improve targeted areas of mood or cognition.

The comparison of research and commercial supplements will highlight whether there are significant differences in dosages or ingredients between formulations used in research compared to over the counter supplements. The resulting findings might indicate the applicability of micronutrient research results to common New Zealand household micronutrient products. This may be informative for those wanting to provide New Zealand parents with information make better choices when purchasing micronutrient supplements. Through this investigation it will also be possible to identify any commonalities across the research and commercial supplement ingredients and investigate possible reasons behind the common inclusion or exclusion of the ingredient(s). An example of this is a vitamin or mineral that is included across all, or almost all supplements. If common components are identified this might provide useful information about mechanisms of pharmacological action, and in turn, possibly provide information for the development of useful products (ie. which have a pharmacological rationale for their activity) in the future.

There may be a number of conceptual frameworks that explain the previous literature findings of behavioural change as a result of micronutrient supplementation, and the potential mechanisms of action need not be mutually exclusive. Inborn errors of

metabolism can have many effects, including influencing enzyme/coenzyme reactions and ultimately brain function (Kaplan et al., 2007). One third of genetic mutations are known to result in an enzyme having decreased binding affinity for a coenzyme, and it is possible that brain dysfunctions such as unstable mood represent a type of genetic mutation, whereby the individual requires higher amounts of specific micronutrients for normal metabolic functioning (Ames, 2004). It is also established that nutrients can alter gene expression so (Kaplan et al., 2007) for example, colorectal cancer patients. Pufulete, et al. (2005) found that a folic acid supplement significantly reversed the inadequate DNA methylation present in the cancer patients, hence altering gene expression.

A further mechanism of action by which micronutrient supplements achieve pharmacological results may be the B vitamins structure activity relationships (SARs) with dopamine (Shaw et al., 2010). Dopamine is involved in a number of psychological disorders including schizophrenia, ADHD, addiction and psychosis (Kapur, 2003; Shaw et al., 2010). The therapeutic effect of Ritalin (methylphenidate) in the treatment of attention deficit hyperactivity disorder (ADHD) is thought to be linked to its effects on norepinephrine and dopamine(Shaw et al., 2010). The motor dysregulation characteristic of ADHD may be attributed to dopamine depletion prefrontal-striatal-thalamic-cortical pathways that project through either the internal or the external segment of the globus pallidus, which leads to difficulty in initiating movement or excess motor activity (Solanto, 2002). Insufficient levels of dopaminergic activity are also believed to be primarily responsible for the cognitive symptoms of the disorder. This is hypothesised due to the improvements found when treated with stimulants such as methylphenidate that may reduce dopamine depletion (Mchta et al., 2001). The formulae found to effectively ameliorate the symptoms of ADHD following long-term dosing, include an array of B vitamins, biotin and related compounds (Shaw et al., 2010). An example of this outlined by Shaw et al. (2010) where they postulate that vitamin B_1 may occupy the dopamine transported (DAT) binding site, reducing the efficiency of dopamine transport from the synapse. This increases the synaptic dopamine level, consequently having pharmacological effects similar to methylphenidate (Ritalin©). This means that vitamin B_1 may behave pharmacologically in a similar manner to methylphenidate and thus ameliorate the symptoms of ADHD.

Of the B vitamins, three; namely B_6, B_9 and B_{12}, have been linked to reductions in homocysteine levels (NHMRC, 2006). Homocysteine is a natural amino acid synthesised at a particular point of the methylation process. Methylation denotes the addition of a methyl group to a substrate, or the substitution of an atom or group by a methyl group. An oversupply or accumulation of homocysteine has been directly linked to heart disease and depression related symptoms (Folstein et al. 2007).

It is clear that there are a number of possible mechanisms of action that may be responsible for the observed psychological effects of micronutrient treatment, and these mechanisms may vary across different nutrient combinations. Future exploration of these potential mechanisms of action is vital to providing effective treatments with the best possible outcomes for an individual's circumstances.

1.1. Research on the Use of Micronutrients.

A 1997 survey of American children indicated that 54% of all three year olds are given a dietary supplement, and of those children, 85.4% are given a micronutrient supplement (Yu et al., 1997). Yu et al. (1997) also showed that the child health characteristics associated with supplement use included first birth order, having selective eating behaviours or poor appetite, or chronic health problems. In a US based study, Rock (2007) found adolescents to have a lower use of micronutrient supplements and dietary supplements in general. They also found adolescent supplement use to be associated with being female, having a lower intake of total and saturated fat and higher dietary nutrient intakes. Maternal characteristics found to be associated with child micronutrient supplement use are mothers that are older, more educated, have greater household income, take supplements during pregnancy, and are non-Hispanic white (Yu et al., 1997). Unfortunately, these investigations suggest that youths that may have a greater risk of nutrient deficiency due to their socioeconomic (SES) circumstances, are less likely to take a supplement.

The European Prospective Investigation into Cancer and Nutrition (EPIC) study analysed the dietary intake of persons aged between 35 and 74 years in 10 western European countries (Olsen et al., 2009). These countries included Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, the Netherlands and the United Kingdom. They found that the most systematic variation in dietary food intakes (excluding supplement

use) related to the B vitamins. Across the 10 countries and almost all regions within these countries, after adjustment for energy intake and body composition, men were found to have substantially higher B vitamin intakes than women. Olsen et al. (2009) found that education has also linked to vitamin intake, although in this case dietary intake excluded supplement use. Olsen et al. (2009) showed that education was positively associated with vitamin C intake in both men and women and to vitamin B_6 intake in women.

In summary, research has found that micronutrient use is common, and adults and adolescents with suboptimal nutrient intakes from food sources are less likely to be dietary supplement users. Research to date suggests that a large portion of children, ie. approximately 46% (Yu et al., 1997) take a micronutrient supplement; therefore, it would be useful to understand parental motivation for giving a supplement to their children. Scientists have showed the percentage of children taking micronutrients, and the demographics of the child and the parent, but not what motivates parents to purchase a micronutrient supplement. If parents are motivated to buy a supermarket or pharmacy micronutrient supplement based on the belief they provide mental or emotional benefits for their child, it is also important to examine the validity of these beliefs.

1.2. Current Study Purpose

The purpose of this study is to explore the answers to two key questions. Firstly, through product comparisons previously mentioned, establish if the micronutrient products designed for children that are sold over the counter in New Zealand are likely to provide any mental or emotional benefits to our children, through a comparison with the micronutrient research to date. Secondly, to identify the motivations of New Zealand parents when they purchase a micronutrient supplement for their child. This part of the research will be conducted in the form of an on-line survey. The survey will also attempt to identify the micronutrient brands of choice of New Zealand parents, factors that influence their purchasing, and identify any benefits that parents have perceived as a result of their child's micronutrient use.

The two main components of this research are exploratory as there has been no previous investigation into these specific areas. For part one of this study, the investigation was based on a brief preliminary examination of research and commercial supplements. It

was hypothesised that the dosages used in micronutrient studies would have different ingredients and average dosages higher than the commercial dosages in micronutrient supplements. The investigation for part two of this study was based upon initial questioning of parents as to why they brought a micronutrient supplement for their child. These preliminary questions led to the hypothesis that the majority of parents in New Zealand were not purchasing a micronutrient supplement to improve their child's psychological well-being.

2. Mental Health Micronutrient Literature Review

The formulation and proven efficacy of safe and well tolerated effective treatments for psychological disorders and mood and cognition, is a priority of both practitioners and researchers, however psychologically focussed randomised placebo controlled micronutrient trials for children remain relatively limited. A review of the micronutrient research that has been conducted with the youth population indicates improvements in symptoms of bipolar disorder (Rucklidge et al., 2010; Kaplan et al., 2004), schizophrenia (Joshi and Eswaran 1980), and autism (Mehl-Madrona et al., 2010). Other benefits resulting from micronutrient administration have also been found in mood and general behaviour (Kaplan et al., 2002; Kaplan et al., 2004), and IQ (Schoenthaler et al., 1991; Benton, & Cook 1991).

After a search of the scientific literature, each of the following sections outlines the research conducted into the effects of micronutrient supplements on children as discussed above. The lack of randomised controlled trials meant that to obtain the best indication of micronutrient effectiveness, all types of studies were included in the analysis. Overall, the findings were generally positive, both the studies that found a positive effect, and those that found a non-significant or negative outcome, are outlined in each section.

2.1. Paediatric Bipolar Disorder (BPD)

BPD is a psychiatric mood disorder characterised by periods of elevated mood clinically labelled as mania, sometimes accompanied by periods of depressed mood. Micronutrient treatment has been found to lead to a reduction in a number of paediatric

bipolar disorder symptoms. There have been a total of three studies. Of these three studies all found a reduction in symptoms. One of these studies did not use psychometrics to measure this change; consequently significant reductions are outlined for two of the three studies. Micronutrient supplementation has been found to lead to symptom reductions in hallucinations, sleep problems, tantrums, depression, mania, compulsions, mood and anxiety. All three of these micronutrient BPD studies used a micronutrient product called EMPowerplus.

EMPowerplus is the most frequently used supplement in psychologically focussed micronutrient research. It is a 36 ingredient, broad spectrum micronutrient formula that includes vitamins, minerals, and plant nutrients, apparently designed to provide nutritional support for the central nervous system. A safety and tolerability review that incorporated the findings from thirteen different reports of mental health research involving EMPowerplus was recently published (Simpson et al., 2011); they found the micronutrient formula EMPowerplus to be associated with no occurrences of clinically meaningful negative outcomes, and only minor transitory physical side effects such as headaches or nausea. The one experiment that allowed for direct comparison between the micronutrient treatment group and the medication group, found significantly fewer adverse events and less weight gain in the micronutrient group compared to the medication group (Simpson et al., 2011). They also highlighted that EMPowerplus was consistently related in the literature to an enhanced response to pharmaceuticals, especially for patients with depression or bipolar disorder.

The case study that did not use psychometrics to document change, (Frazier et al., 2009) was based on a boy diagnosed with bipolar disorder at age six. The boy's disorder had escalated in severity and he had developed psychotic features, generalised anxiety and obsessive-compulsive disorder (OCD) by age ten. His conventional medication was changed often due to intolerable side effects or inadequate treatment response, and no medication maintained a desirable mood balance or a consistent improvement in symptoms over an extended period of time. At age 12 over the period of a month, he was transitioned off his psychotropic medications and onto a full dose of EMPowerplus. Following this transition period his global functioning notably improved, his sleeping, peer interactions, anxiety and focus improved, his compulsions decreased and hallucinations ceased. His parents stated that the improvements in his functioning were greater than those he made in the past on

other medications. In the subsequent nine months these symptom improvements were maintained, allowing the child to attend public school for the first time. Although standardised data collection did not occur in this case report, the longitudinal nature of the clinical record supports the observed effects of EMPowerplus.

Rucklidge, et al. (2010) analysed the data provided by people who purchased EMPowerplus for their children under the age of18. The 120 participants had been previously diagnosed with either PBD or PBD with ADHD. Data was analysed from three to six months post baseline. In some cases medications were reduced as the micronutrient supplement was introduced. The median dose of the micronutrient formula at the Last Observation Carried Forward (LOCF) was 13.7 capsules daily. The LOCF for those with PBD indicated a 46% decrease in symptom severity from baseline (effect size = 0.78 cohen's d, $p < 0.001$). For those children with PBD and ADHD, symptom severity reductions from baseline were similar to those participants with PBD alone, with a 43% reduction in PBD symptoms and a 40% reduction in ADHD symptoms. These findings were consistent across both age and gender. This study was limited by its open label nature, the inherent self-selection bias, the use of parent report only, and the lack of a control group. The results however, suggest micronutrients may enable children to reduce their psychiatric medications, and improve their psychiatric symptoms with minimal side effects.

Frazier et al. (*in press*) conducted an open label micronutrient trial using EMPowerplus that involved children between the ages of 6 and 12 years with BPD. They found significant decreasing trends in both depression and mania from baseline, during eight weeks of micronutrient administration. From the beginning of treatment through to the final visit, a 37% decrease in depression scores ($p< 0.06$) and a 45% decrease in mania scores ($p< 0.01$) were revealed by intent to treat analysis. Minor temporary side effects were experienced, most often in the form of gastro discomfort.

Overall results suggest micronutrients may provide a reduction in a number of paediatric bipolar symptoms, although from this research it is not clear which symptoms may be most sensitive to micronutrient supplementation. Clearly, much more research is needed in this area, as preliminary studies indicate micronutrient supplements may provide significant improvements in symptoms, with limited side effects.

2.2. Autism Spectrum Disorder (ASD)

Autism Spectrum Disorders (ASD'S) are heterogeneous neurodevelopmental disorders. ASD's are complex disorders with a strong genetic component, and are likely to have a number of causes, (Skaar et al 2005). Autism has is becoming increasingly more common, highlighted by a recent study which identified that approximately 1 in 91 children in America is diagnosed with an ASD (Kogan et al., 2007). Therapeutic intervention in this disorder varies according to individual circumstances. Treatments with vitamins, some amino acids, minerals and other nutritional supplements have recently emerged as effective treatment options for ASD symptom reduction for some children (Adams, 2007). These treatments may be effective because psychiatric symptoms in ASD may represent an inborn metabolic dysfunction which is associated with slowed metabolic activity due to suboptimal availability of micronutrient cofactors (Ames et al 2002).

Children with autism are particularly at risk for nutrient deficiencies in a range of nutrients essential for brain function, largely due to the abnormal self-restrictive eating habits that this population tend to demonstrate, often resulting in reduced intake of a wide variety of foods. Through blood test analysis, Adams, et al. (2003) found that children with ASD had on average much lower levels of most vitamins: vitamins A, C, D, and E and all B vitamins except choline, when compared to age-matched controls.

The most successful and rigorously tested of the vitamin and nutritional therapies is a vitamin B_6 (pyridoxine) and magnesium combination (Rimland 1987; Rimland, 1988; Martineau et al 1988). Vitamin B_6 is required for over 100 enzymatic reactions, including the production of major neurotransmitters such as serotonin and dopamine, and glutathione which is required for detoxification (Rolfes et al., 2006). Magnesium is used in this treatment setting to prevent the possibility of hyperactivity, which can occur if vitamin B_6 is taken by itself. The effectiveness of this treatment could be related to the actions of both vitamin B_6 and magnesium as nutrients themselves, or the mechanism of action for these nutrients may be due to their influence on reactions that affect a number of neurotransmitter systems which may be implicated in autism (Martineau et al 1985). The high dose B_6-magnesium combined studies found an average of around 45-50% of children and adults with autism benefited from the treatment (Pangborn et al., 2005).

In the most recent micronutrient studies the effects of nutrients on ASD symptoms are further supported. There have been four micronutrient studies, all of which have found a positive effect. These studies are in a variety of different forms including a case study, a naturalistic open label case study and two randomised placebo controlled trials. The case study involved an un-medicated nine year old boy with ASD (Xia, 2011). Xia (2011), found that scores on the Autism Evaluation Checklist reduced from baseline following five months of supplementation by 47.6% and 53.1%; as rated by two independent assessors. The supplement contained an amino acid analogue called dimethylglycine (DMG; 375 mg daily), vitamin B_6 (pyridoxine HCl; 37 mg daily) and magnesium (magnesium citrate-glycinate-oxide; 180 mg daily). A noticeable change in the boy's behaviour was also reported by his school teachers and parents. Two years since the beginning of nutritional supplementation the participant's symptom improvements were retained with no-side effects observed. Although these results cannot be generalised, the findings provide evidence that support the effectiveness of using nutritional supplements when treating ASD.

In a group of typical children not taking supplements and of a similar age pre-supplementation vitamin B_6 levels were measured by Adams and Hollaway (2004) in both the placebo and supplement group. Prior to taking the supplements, the placebo and supplement group had similar vitamin B_6 levels which were well above the typical reference range for typical children at this age. The typical reference range was consistent with the average level of B_6 in the typical children whom were tested. The difference in total vitamin B_6 levels between the ASD group and the typical children was highly significant ($p < 0.001$). This elevated level implies a functional need for more vitamin B_6 in those with ASD's, and may explain why high doses of vitamin B_6 have been shown to benefit children with an ASD.

In a randomised, double blind, placebo controlled trial Adams and Holloway (2004) administered Spectrum Support, a supplement available on the internet direct from the company BrainChild Nutritionals, which contains a broad array of vitamins and minerals. This supplement was administered over three months to eleven children with ASD (Adams & Hollaway, 2004). The mean age of the eleven participants and of the nine controls was 5 years of age. No adverse side-effects were reported when the dosage instructions were followed. At the end of the study there were no significant improvements in any areas of the Global Impressions scale in the placebo group. Those children who received the

supplement had significant improvements in their sleep and gastrointestinal symptoms ($p < 0.05$).

Adams, et al. (2011) conducted a randomised, double-blind, placebo controlled trial with a micronutrient supplement that was administered over 3 months to 141 children and adults with autism. The overall average age of the participants was between 9 and 13 years old. Of the 141 participants, 53 were children aged between five and sixteen and had their nutritional and metabolic status measured pre and post treatment. The comprehensive supplement contained most vitamins and minerals and did not include iron or copper, as the researcher's had determined from previous research that these two minerals were not needed by most children with autism. The dosage of B_6 was deliberately set high at 40mg. This is high when compared to the New Zealand recommended daily allowance (RDA) for $B_6$of 1mg. At post-test the supplement group demonstrated significantly greater improvements than the placebo group on the Parental Global Impressions-Revised (PGI-R) ($p < 0.01$), and on the sub-scores of hyperactivity ($p < 0.01$) and tantrums ($p < 0.01$). The PGI-R was used because it assesses changes in symptoms. On three additional measures there were no significant differences between the supplement and placebo group. The nutrition and metabolic status of the children measured in the supplement group was found to significantly improve to normal or near normal levels in the areas including methylation, glutathione, oxidative stress, and sulfation.

EMPowerplus or a supplement customised to match EMPowerplus was used by Mehl-Madrona et al. (2010) in a naturalistic open label case study of children with ASDs. The trial consisted of two well matched groups: the micronutrient group (44 participants) and the medication group (44 participants). If already on medication the participants in the treatment and comparison groups continued their normal medication throughout the trial. The mean age of the groups was between eight and nine years of age. The micronutrient group received EMPowerplus (or similar), and were found to have significantly greater symptom declines in a range of areas when compared to the medication alone group. Areas where the change from baseline was significantly greater for the micronutrient group than the medication group included activity level, withdrawal, angry affect and unspontaneous relation to the examiner. The micronutrient group's improvement on the Aberrant Behaviour Checklist was significantly greater than that of the medication group ($p < 0.0001$), the same was true on the Clinical Global Impressions scale ($p < 0.01$). A significant reduction

in self-injurious behaviour intensity was found in the micronutrient group and not the medication group after the final appointment ($p < 0.01$). There were no areas of symptomology that improved significantly more in the medication group than the micronutrient group. Overall side effects including adverse events and weight gain were also much less in the micronutrient group with 33 adverse events in the micronutrient group compared to 214 recorded in the medication group. At the end of the trial the number of medications consumed by the two groups was significantly different ($t = -6.19$, $p < 0.0001$). The mean number of pharmaceutical pills consumed by the micronutrient group was 0.59 daily (SD =0.95), in contrast the mean number for the medication group at the end of the supplement administration period was 2.23 daily (SD=1.48). This study highlights a number of possible benefits resulting from micronutrient supplementation. Benefits include improved symptoms, reduction of reliance on pharmaceutical medication, and a reduction in adverse side effects when used to treat children with ASDs.

Autism is a complex disorder. There are however, many biomedical abnormalities that have been identified, and although it is unlikely that there will be one general metabolic therapy that would improve symptoms in all cases of ASD, micronutrient treatments for autism appear to be effective. The evidence so far suggests micronutrients are a legitimate treatment used alone, or as a supplementary treatment for some children with ASD's. Further research is needed to verify the efficacy of these treatments and identify those with ASD who will respond best to nutrient supplementation.

2.3. Attention Deficit Hyperactivity Disorder (ADHD)

ADHD is characterized by problems with inattention, hyperactivity, and impulsivity and is one of the most prevalent developmental disorders in childhood. Finding effective treatments with minimal side effects is a goal of both researchers and practitioners. Prevalence rates of ADHD in Australia were estimated to be around 11% in 2011 (Sawyer et al., 2001), and around 4.4 million school aged children in the US are reported to have a history of ADHD diagnosis, many of whom take medication (Bloom & Cohen, 2007). ADHD normally manifests before the age of seven, and the problems associated with this disorder include adverse effects on school performance and peer and family relationships. ADHD is also associated with cognitive deficits, specific learning disabilities, poor self-esteem and

more than half of these children experience co-morbid psychiatric problems (Biederman, 1997).

There have been three studies involving micronutrients in this area. Of these studies two have found significant positive effects, and one found no added benefits resulting from supplementation. The first of these studies directly compared pharmaceutical medication with a micronutrient supplement. Harding, Jadah and Gant (2003) compared the symptom changes in 20 children with ADHD between the ages of 7 and 12. Ten children were self-selected into the Ritalin© treatment group; the other ten were self-selected into the dietary supplement group. The supplement used in the alternative treatment group was specifically created for the trial and contained a multitude of vitamins and minerals, essential fatty acids (EFAs), phospholipids, probiotics and amino acids. The Intermediate Visual and Auditory/Continuous Performance Test (IVA/CPT) was the primary outcome measure used to measure symptom change. The IVA/CPT assesses response inhibition and attention problems, and unique to this test measures both auditory and visual distractibility. This test has high reliability and validity in diagnosing and assessing ADHD treatment efficacy as well as medication titration. After four weeks of treatment, comparative analysis found there to be no significant differences in the level of improvement between the Ritalin© and supplement groups. Both groups showed significant gains ($p < 0.001$) on the full scale response control, and full scale attention control quotients. Despite the possible self-selection bias in this research, the results indicate that micronutrient supplements may have similar effectiveness to Ritalin© in the treatment of ADHD symptoms.

There have been limited placebo controlled trials investigating the effects of a micronutrient supplement on ADHD symptoms. In one placebo controlled trial, the above findings are supported by Katz et al. (2010). They found that treatment with a broad base micronutrient supplement called Nurture and Clarity, led to significantly greater ADHD symptom improvements when compared to a placebo group. The 120 participants were randomly assigned to the treatment or placebo group in a two to one ratio respectively. Participants were children aged between 6 and 12 years of age, and were newly diagnosed with ADHD and had no history of previous ADHD treatment. Participants were excluded if they did not meet the symptom severity threshold set, or if they had any additional medical conditions or illnesses, any co-morbid psychiatric conditions or were using any type of medication. This randomised, double blind, placebo controlled trial was conducted over four

months. The micronutrient formula contained EFAs, phospholipids, amino acids, B-vitamins, minerals and other micronutrients. At the four month follow-up, the treatment group demonstrated highly significant improvements ($p < 0.001$) in all four dimensions of the Test Of Variables of Attention (TOVA: a test used to detect changes in the variables of attention) as well as the overall TOVA score. These findings were in contrast to the placebo group, where no significant changes in any of the test dimensions were found. After adjustment for age, sex and baseline TOVA score, treatment differences between the groups in each of the four subscales persisted strongly. The most significant group differences were found in response time and variability. Throughout the trial no serious adverse events were reported, and any mild, transient adverse events reported did not persist past the first two weeks. At follow-up, 73 participants remained in the treatment group, and 19 children remained in the placebo group, a statistically different completion rate ($p < 0.0001$), which suggests that participants possibly perceived their lack of improvement in the control group and consequently guessed their group allocation. Importantly, the baseline characteristics of the two groups were similar, which helps to alleviate the possible concern of selection bias. This study provides further evidence that micronutrient treatment may provide a safe, well tolerated therapy that effectively improves the symptoms of ADHD, increasing its potential as a valuable ADHD treatment option.

Further research is required to replicate the findings in the discussed micronutrient ADHD studies, this need is highlighted by by Sinn and Bryan (2007) who found no additional symptom improvements when a multivitamin supplement was added to a polyunsaturated fatty acid (PUFA) supplement for ADHD children. The micronutrient supplement administered contained 12 vitamins and 7 minerals. The vitamin dosages used were comparable to over the counter commercial supplements. Sinn and Bryan hypothesise that the absence of additional benefits was likely contributable to the low multivitamin dosages used. They speculate that the dosages were too low to result in any significant changes in a clinical sample. Further research is needed to identify the specific nutrients, and the dosages in micronutrient supplements that are effective in ameliorating the symptoms of this clinical population.

2.4. Mood & General Behaviour

There have been a limited number of placebo controlled trials in the area of micronutrient formulas, but a variety of types of studies provide important links between micronutrients and their effect on mood symptoms. There have been three micronutrient studies, including a case study, a case series and one randomised placebo controlled study. All of these studies reported positive results. As only two of the three studies collected quantitative data, significant effects resulting from micronutrient treatment are discussed for only two of the three studies.

The case study had an open label ABAB reversal treatment format. Kaplan et al. (2002) found that micronutrient treatment lead to reductions in mood lability and explosive rage. Two boys were given the old formulation of EMPowerplus and at full dosage they were taking eight capsules four times daily and were on no medications throughout the duration of the case study. The first subject, an eight year old boy, had been previously diagnosed with atypical OCD, ADHD, mood lability and explosive rage. The second boy, 12 years of age, had been diagnosed with pervasive developmental disorder with Asperger characteristics, and exhibited severe ADHD, learning problems, mood problems and explosive outbursts. To assess symptom change, parents evaluated their children's behaviour on a modified Connors Parent Rating Scale. The two items that were measured were: mood changes quickly and drastically; and temper outbursts, explosive, and unpredictable behaviour. A minimum of one week baseline monitoring preceded the introduction of the micronutrient supplement. Mood, angry outbursts and obsessional symptoms that improved when initially receiving the supplement, returned to baseline levels when not taking the supplement, and remitted when the micronutrient product was reintroduced. No adverse effects of the micronutrient supplement were noted by either the children or their parents. The second boy did however begin to struggle with taking the large number of capsules daily. The new version of EMPowerplus addresses this problem, as the volume of pills required at a full daily dosage has been greatly reduced.

Remaining on a maintenance dose of just eight capsules daily (25% of the full dose) the improvements in these symptom areas were maintained two to three years following the beginning of the trial. Two years following the treatment initiation the second boy began a dose of 15mg dextroamphetamine to help in focus on school days, suggesting that

the micronutrient supplement alone was not sufficient to address his inattention specifically. The clinical effectiveness of this micronutrient supplement is strongly supported by the withdrawal and reinstatement of the supplement and the supporting changes in mood and behaviour. Importantly, the long term stabilisation of mood and behaviour changes achieved with a lower maintenance dose also means that the initial large number of capsules taken daily is not necessary to maintain symptom changes for the long term.

In further support of the Kaplan et al. (2002) case study, is an open label case series on nine children aged between eight and fifteen years of age with mood and behavioural problems. The participants were clinically diagnosed with an anxiety, mood, or behavioural disorder, and had a well-documented clinical history of symptomatology, and were all on a stable psychiatric medication regimen. The micronutrient supplement administered was the old version of EMPowerplus and the full dose given was eight capsules taken four times daily for eight weeks. As measured on the Child Behaviour Checklist (CBCL) statistically significant improvements ($p < 0.01$ on five of the subscales: withdrawn, thought, attention, delinquent and aggression; $p < 0.05$ on two subscales: anxiety and social) were found on seven of the eight CBCL subscales. The participants also showed statistically significant improvements on the Youth Outcome Questionnaire, and the Young Mania Rating Scale. All effect sizes were relatively large at over 0.8 (Cohen's d). No participants discontinued supplement use due to adverse effects; however, the two participants who were taking psychiatric medication experienced moderate excitation and agitation, but this was not reported by any of the children who were not taking psychiatric medication. The largest limitation of this study was the possible expectancy effect, as parents were the sole observational rater during the trial period and they were aware that their child was taking the supplement. The pervasive improvement on these multiple outcome measures and the magnitude of effect sizes however, strongly supports the value of further systematic efficacy research.

In the first study involving typical school children and the effects of a low dose vitamin-mineral supplement on violence and anti-social behaviour, Schoenthaler and Bier (2000) administered a Klaire Laboratory supplement, a low dose vitamin-mineral supplement for four months to 196 school students. The total number of participants was 468. The participants were from two 'working class' primarily Hispanic schools aged between six and twelve. These participants were randomly assigned in a double-blind

fashion to either the placebo or supplement group. The supplement contained 50% of the U.S. RDA of a number of vitamins and minerals other than vitamin C which was increased to 40 mg. The researchers aim in giving this supplement was to raise the vitamin-mineral intake of the participants to the levels recommended at the time by the National Academy of Science for children in this age group. There were 80 students who completed the trial and were disciplined during the time period. Half of these children were from the supplement group. These 40 disruptive school children from the supplement group were involved in 47% less serious rule violations during the four month trial period when compared to 40 similarly disruptive schoolchildren who were given placebos. This group also had lower rates of eight types of recorded infractions, including threats/fighting, disorderly conduct and endangering others. Only one of the 40 children who received disciplinary action during the intervention period committed three or more offenses, while nine of the forty children taking the placebo tablets committed three or more offenses. Importantly, the 47% difference in anti-social behaviour between the supplement and placebo groups is accounted for by the presence of these nine habitual offenders in the placebo group. Correction of nutrient intake, usually corrects the low concentrations of vitamins in the blood and improves brain function, however deficiencies would not have been corrected with the placebo pills. Schoenthaler and Bier speculate that this is evidence that for the minority (habitual offenders), undiagnosed and untreated malnutrition is likely to have impaired their brain function to such an extent that normal learning from discipline did not occur. A similar reduction in anti-social behaviours has also been found in adult and juvenile inmate populations (Gesch et al., 2002; Schoenthaler, 1985a; Wolfgang et al., 1972), lending further weight to the role of nutrient intake correction in significantly reducing anti-social behaviour in both older incarcerated subjects with histories of antisocial behaviour and normal populations of younger disruptive children in an educational setting.

These results indicate that micronutrients are likely to be effective in moderating a number of mood or general behaviour variables including anxiety, mood or behavioural disorders, drastic mood changes, unpredictable behaviour, explosive outbursts and antisocial behaviours. Further testing is required to identify the specific areas within mood and behavioural disorders for which micronutrients are most effective, and the specific mixture of nutrients that are most effective at ameliorating mood and behavioural symptoms.

2.5. Cognition

Cognition appears to be the most common area of interest and conflict over mechanisms of action, in research investigating the effects of micronutrients for children. A common school of thought is that significant improvement in intelligence quotient (IQ) is only found in those children who were poorly nourished prior to supplement administration (Schoenthaler, & Bier 1999; Benton 2001), and that the large improvement in these few poorly nourished children, is responsible for the significantly greater IQ increases in treatment groups, for example found in Schoenthaler, et al. (2000) and Schoenthaler, et al. (1991). Micronutrient studies that investigated the effects of supplementation on cognition in children are outlined in the following section, including two studies that did not find significant cognitive improvements following micronutrient supplementation.

Schoenthaler, et al. (1991) conducted a randomised placebo controlled trial with school children aged between 13 and 16, however only non-verbal IQ was measured. The 26 delinquent participants were measured pre and post treatment on the Wechsler Intelligence Scale for Children-Revised (WISC-R). Those participants randomly assigned to the supplement group received a Klaire Laboratory supplement for the 3 month trial period. Following the trail period, significant increases were found in the non-verbal IQ ($p<.001$) of the supplement group. No significant non-verbal IQ change was found in the placebo group. This difference in IQ gain was found however, to be attributable to 4 of the 15 children who took the active micronutrient tablets. The remaining 11 supplement group participants were found to have an IQ change at post-test that was closely matched to that of the placebo group. Through examinations of pre-test nutrient status, the four respondents responsible for this group difference in IQ change, were found to have low water-soluble vitamin concentrations in their blood, this was not found in the remaining 11 respondents in the supplement group. Pre-test brain electrical activity mapping on six children with low concentrations of blood vitamins was conducted by a neurologist who was blinded to participant treatment status. Prior to the study all six children were found to have abnormal electroencephalographic (EEG) activity. The two children from the abnormal EEG group who received placebos demonstrated no improvement in EEG activity at post-test. The four who received the micronutrient supplement had markedly improved EEG activity, with a reduction of EEG activity abnormalities from 14 to 2. Schoenthaler et al.'s (1991) results

support the theory that gains in nonverbal IQ would be found among poorly nourished children.

Schoenthaler et al. (2000) conducted a randomised double-blind, placebo controlled trial involving 245 Arizona school children aged 6 to 12 years. Children were randomly assigned into the supplement or placebo group, and pre-test screening showed the supplement and placebo groups had no significant differences in age, gender, race or pre-test IQ score. The supplement, administered over 3 months, was a low dose micronutrient, which provided 50% of the U.S daily recommended allowance of vitamins and minerals. Post-test nonverbal IQ as measured by the WISC-R, found a 9.97 point IQ gain in the supplement group, and a 7.5 point IQ gain in the placebo group. The difference in IQ gain of 2.47 points was found to be significant ($p < 0.05$). Further analysis revealed the gain could be contributed to a minority of children who produced IQ gains of over 15 IQ points. They attribute this large increase in IQ found in the minority of children, to poor nourishment before supplementation.

A two-by-two factorial randomised placebo controlled, double blind trial was conducted to investigate the combined effects of micronutrients and essential fatty acids on cognition in school children (Osendarp et al. 2007). This study consisted of four participant groups: 1) received multivitamins; 2) received docosanhexanoic acid (DHA) and eicosapentaenoic (EPA); 3) received multivitamins, DHA and EPA; and4) received a placebo. The study was carried out over one year, with participants receiving their supplement or placebo 6 days a week. The participants were aged between 6 and 10 years of age, 396 from Adelaide, Australia and 384 from Jakarta, Indonesia. Pre-test bio-chemical analysis revealed Australian participants to be generally well nourished and the Indonesian participants to be in general under nourished. The micronutrient treatment groups in Australia were found at post-test measurement to have significant improvements in scores representing verbal learning and memory with an estimated effect size of 0.23 (95% CI: 0.01, 0.46). A similar trend although non-significant was found amongst the Indonesian girls, for whom the estimated effect size for the verbal learning and memory scores was 0.32 (CI: -0.01, 0.64). The addition of DHA and EPA to the multivitamin supplement was not found to result in beneficial effects on cognitive performance. This study suggests that supplementation with multiple micronutrients can result in improvements in verbal learning and memory in well-nourished school children. This is contradictory to the previous findings of Schoenthaler, et

al. (2000 & 1991) of large improvements in IQ of under nourished children, and no significant IQ change in children who are well nourished following micronutrient supplementation. This clearly highlights the need for further research that uses micronutrient supplements with consistent compositions and the use of similar IQ measurement tools to clearly define the role of micronutrients in cognition.

Benton and Cook (1991) used a Larkhall Laboratories supplement in their randomised double blind, placebo controlled study, which investigated the effects of six to eight weeks supplementation on a number of intelligence measures. The 47 participants were all six years of age. The post-test intelligence scores revealed an average 7.6 point increase in IQ in the supplement group, which was found to be a significant increase ($p < .001$). No significant change in IQ was found in the placebo group. After an examination of the subscales, it was found that the significant changes in IQ at post-test measurement for the supplement group were primarily on non-verbal measures. This finding is of theoretical importance when looking at how micronutrient supplementation may result in improved cognition. Verbal IQ tests are largely measures of crystallised ability and non-verbal IQ tests are measures of fluid ability (Cattell, 1943). Benton and Cook (1991) postulate that if poor diet was inhibiting and micronutrient supplementation was facilitating neurochemical efficiency, then as they found, it would be fluid intelligence that would be expected to be stimulated, which may be one way in which micronutrient supplements can lead to improved cognition. Post-test scores also revealed that the children who received supplements were more likely than the placebo group to concentrate on the task ($p < .05$) and less likely to fidget ($p<0.05$). The researchers suggest that this may be evidence of micronutrient supplementation improving the mood of those with an inadequate diet.

Indian researchers Kumar and Rajagopalan (2008) also investigated the effects of micronutrient supplementation on school children. The participants aged between 7 and 11 years old were randomly assigned to either: 1) the control group, 72 participants; or 2) the micronutrient group, 51 participants. The experimental group consisted of school boarders only, and the micronutrient supplement was delivered in their food. Precautions and dose adjustments were made in order to protect the integrity of the micronutrient supplement cooked into the food for the experimental group participants. The school was chosen from a list of schools with the minimum number of intervening holidays, in order to limit the number of days where the children would go home, which would interrupt treatment.

Following one year of supplement administration, the mean improvement in five out of the seven memory and attention scores was found to be significantly greater in the experimental group than the mean change in the control group ($p < .05$). In the overall IQ score measured by Ravens progressive matrices, no significant improvements however were noted for either group. The haemoglobin, haematocrit and red blood cell count significantly improved in the experimental group following supplementation ($p <.05$). In contrast, a significant decline in haemoglobin and red blood cell count was discovered at post-test in the control group. Kumar and Rajagopalan link the IQ measurement findings and blood test results, suggesting that iron deficiency anaemia can be improved and that this can result in improved scores for children with lower scores on tests of cognition. This is a broad statement however, that needs further exploration.

In a different approach to micronutrient enhancement of cognition, Sandstead, et al.'s (1998) interest was in the effects of zinc of cognition. They conducted a trial with 740 urban low income Chinese children aged between six and nine years of age. Outcomes were measured at baseline and after the test period of 10 weeks. This trial had no placebo group. The three treatment groups consisted of: 1) received zinc; 2) received zinc and a micronutrient supplement; and 3) received a micronutrient supplement. The micronutrient supplement used in this trial was specifically created to best compliment the effects of zinc, for example the folate level was set at 25% of the RDA of the National Research Council (National Research Council, 1989), and the following minerals were excluded due to the possibility of interference with the intestinal absorption of zinc: iron, calcium, magnesium and phosphorus. Following treatment, which was administered six days a week for the 10 week trial period, neuropsychological performance was measured by tasks from the Cognition-Psychomotor Assessment System-Revised (CPAS-R). Neuropsychological performance was associated with more overall improvement in the zinc plus micronutrient group than in the zinc or micronutrient groups. The significant differences between these groups ($p <.05$) were noted on measures of concept formation, abstract reasoning, and circular tracking (a measure of sustained attention). The significant improvements in neuropsychological performance found in the participants who received zinc and a micronutrient supplement, suggest that zinc alone is not the most effective cognitive enhancer, and that the repletion of other micronutrients is also necessary when aiming to achieve significant improvements in cognitive performance.

Cognition can also improve in atypical child populations following micronutrient supplementation. Harrell et al. (1981) investigated the effect of eight months of micronutrient supplementation on 16 children with Down syndrome. Five of the children received the active supplement, which contained eight minerals in moderate amounts and 11 vitamins in large amounts. The remaining 11 children received a placebo. The improvement in IQ at four months was found to be significantly greater in the supplement group compared to the placebo group ($p<.05$). The significant improvement in IQ was maintained in the supplement group after eight months supplementation, with results indicating a significant gain in IQ ($p <.001$). These findings indicate that micronutrient supplements may be useful when aiming to improve cognitive in a wide range of children.

In contrast to the before mentioned cognition studies that found positive significant results as a result of micronutrient supplementation, Perlman, et al. (2010) and Nelson, et al. (1990) did not find significant improvements in cognition following supplementation. Perlman, et al. (2010) investigated the supplement effects in New Jersey, United States, of a low dose micronutrient supplement on grade point average change, late arrivals to school and school days absent. The study was randomised, double blind, and placebo controlled and contained 640 participants aged between 6 and 12 years old. The multivitamin administered in this study was designed to be equivalent to a standard over the counter multivitamin supplement. The ingredients and doses used in this supplement were not however, provided in the published research, and were not able to be obtained through attempted correspondence with the primary author. The micronutrient and placebo were administered on school days only. Post-test measurement revealed no significant differences in grade point average scores, the number of days absent from school or in lateness to school following four months of the micronutrient supplementation. There are a number of factors that may have led to this non-significant finding: the administration of the supplement exclusively on school days, the low dosage supplement used, the outcome measurements selected (school absenteeism and GPA scores), and the lack of measurement of non-verbal forms of IQ.

Nelson, et al. (1990) investigated the effect of a specifically created micronutrient supplement on the verbal and non-verbal intelligence of typical British school children between the ages of 7 to 12 years old. The randomised, double blind, placebo controlled study consisted of 194 successful participant completers. The supplement or placebo was

administered by teachers during the week, and extra pills were given to the child to administer to themselves in the weekends. Following the 28 days treatment period, no significant differences were found between the experimental and control groups. The limited trial period and the dosages used in the micronutrient supplement may be partially responsible for the lack of effect found. The nutrients included in the supplement were broad, the dosages however, were in general lower than the dosages used in previous cognitive micronutrient research.

The scientific literature indicates that micronutrient supplementation when used to improve the cognition of school children and possibly other a-typical child populations, may have a significant effect on a child's cognitive functioning. The two cognitive studies with non-significant findings however, highlight the need for further investigation into the duration of administration necessary and the best method of measurement for cognitive change.

2.6. Schizophrenia

One study was identified that examined the effect of a micronutrient supplement on the symptoms of schizophrenia. This study found symptom reductions resulting from supplementation. This study was a case report on a 17 year old, drug resistant schizophrenic and manic depressive girl. Weeks (2004) recommended dietary changes and administered a broad based micronutrient supplement specifically tailored to the patient's needs. After taking the mixture of micronutrients for one month, the patient was completely off her medication and felt much better. Weeks (2004) theorised that many of the girl's initial symptoms may have been exaggerated at the outset due to a medical overdose prescribed by her previous psychiatrist, so the symptom alleviation cannot be completely attributed to micronutrient use.

This study provides preliminary indications that micronutrient supplements may be worth exploring further in the treatment of schizophrenia.

Presented in the following section is a description of all of the ingredients included in the supplements in the above mentioned studies, as well as the ingredients included in commercial supplements. This is to provide a brief overview of the key roles and

characteristics of the wide spectrum of micronutrients included in the micronutrient supplements.

3. Key Roles of Individual Micronutrients

The nutrient reference values referred to in the following section include the Recommended Dietary Intake (RDI), Adequate Intake (AI), Upper Level of Intake (UL) and Lowest Observed Adverse Effect Level (LOAEL). The values presented unless stated otherwise are from national Health and Medical Research Council (NHMRC, 2006) designed to guide the public to optimal health and well–being. These guidelines take into account existing food cultures, cultural diversity, sustainability and cost. The RDI value is the dietary intake level sufficient to meet the nutrient requirements of nearly all healthy individuals. AI values are given when an RDI cannot be determined. An AI value is based on observed or experimentally determined estimations of nutrient intakes that are assumed to be adequate. Consequently, AI values can be interpreted with less confidence than RDI values. A UL value is the highest daily nutrient intake level likely to pose no adverse health effects to almost all individuals. Above the UL intake, the potential risk of adverse effects from excessive nutrient intake increases. Members of the general population are cautioned to not routinely exceed UL intakes. The LOAEL is the lowest exposure level at which there is statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and the appropriate control group (NHMRC, 2006).

In the following sections the ingredients of micronutrient supplements are described. Firstly, vitamins are individually discussed. This discussion includes a description of essential roles of vitamins in both mental and physical health, and the New Zealand RDI or AI, UL and LOAEL vitamin dose, generally for children aged between 9 and 13 unless stated otherwise. Secondly, the minerals that appear in micronutrient supplements are described. The RDI, UL and LOAEL doses are presented in Table 1, along with the key physiological role of each mineral. Lastly, other ingredients including amino acids found in micronutrient supplements are presented in Table 2, along with a brief description of their key physiological or nutritional roles.

3.1. Vitamins

Vitamin A is a fat soluble vitamin that plays an essential role in vision, the functioning of a healthy immune system and maintaining normal reproduction and growth. An adequate supply of vitamin A also helps prevent morbidity and mortality from infectious disease, particularly in children (Glasziou & Mackerras 1993). Vitamin A can come in a number of forms including retinol, retinal, retionoic acid or retinol ester. Vitamin A deficiency, specifically retinoic acid and retinal forms of vitamin A, can result in abnormal dark adaptation, xerophthalmia (a serious eye disorder) or blindness. This is uncommon in New Zealand; however the New Zealand Children's Survey 2002 (Ministry of Health 2003) stated that a significant proportion of Pacific children might be at risk of insufficient intakes of vitamin A. The RDI for children aged between 9 and 13 years is 600 µg. The UL for vitamin A as retinol is 1,700µg daily for children aged between 9 and 13. The UL for beta carotene cannot be established for supplement use as no dose-response relationship for the observed effects is available (European Commission, 2000).

Thiamin (vitamin B_1) is a water soluble substance that is essential for converting blood sugar into energy. If intake of thiamin is high, only a small amount will be absorbed with the rest being excreted via urine, with the total body content of the vitamin being around 30mg. Thiamin is also involved in metabolic activities in nerves, heart, and muscles and in the production of red blood cells. There are two major diseases that can result from thiamin deficiency, beri beri and Wernicke- Korsakoff syndrome. In western countries beri beri is seen rarely, with occasional cases found in alcoholics. Wernicke- Korsakoff syndrome is usually found in people with chronic alcoholism who eat very little, as alcohol requires thiamin for its metabolism. This syndrome is associated with severe psychiatric and cognitive symptoms (Mann, 2000).The symptoms of Wernicke's include confusion, lowered level of consciousness and ataxia. Studies where participants have been deprived of thiamin have found a range of outcomes including marked irritability, depression, fearfulness, emotional instability, anxiousness and lower mood (Graham, 2001; Benton 1995; Heseker 1992). The RDI of thiamin for children aged between 9 and 13 years old is 0.9mg. The UL cannot be estimated due to insufficient data, although existing evidence available suggests that current intake levels of thiamin from all sources do not represent a health risk to the general population (Australia and New Zealand Ministry of Health 2006).

Riboflavin (vitamin B_2) is a water soluble vitamin. The bioactive forms of riboflavin are key in the reactions in the catabolism of fuel molecules. It is also important in the body's handling of nutrients including vitamin B_6 and the conversion of tryptophan to niacin. Deficiency can indirectly lead to increased cardiovascular risk, and may contribute to anaemia when iron levels are low (Powers 2003). Riboflavin deficiency can also lead to eczema, cracked skin, a burning sensation on the tongue and eye irritation. The RDI for children aged between 9 and 13 is 0.9mg daily. The UL for riboflavin cannot be estimated as no adverse effects have been associated with consumption in food or supplements, and those studies that have been undertaken with large doses did not systematically assess adverse events (Schoenen et al. 1998).

Niacin (vitamin B_3) plays a role in the intracellular respirations system and with enzymes involved in oxidation of fuel substrates. Essentially due to its role in energy metabolism the amount of niacin required is related to individual energy requirements. Niacin is a vasodilator, this means that it acts to widen blood vessels therefore increasing blood flow. A deficiency in niacin can result in the disease pellagra, associated with inflammation of the skin, diarrhoea, depression, thinning of the hair and in severe cases, delirium. Malnourished persons are at risk for developing niacin deficiency. The RDI for children aged between 9 and 13 years of age is 12mg daily. The UL of intake for niacin is important as even mildly high doses can cause a number of side effects including hot flushes, headaches, itchiness and stomach problems. The UL for children and adolescents aged between 9 and 13 for nicotinic acid is 20mg daily based on a body weight basis. The UL set for the same age group for nicotinamide intake is 500mg daily. This upper limit is set much higher as nicotinamide is not a vasodilator and therefore does not cause flushing.

Pantothenic Acid (vitamin B_5) is a component of coenzyme (CoA) and phosphopantetheine, and its role is important for the metabolism of fats, carbohydrates and proteins. CoA also plays an important role in the production of steroid hormones and the synthesis of vitamin A and D, and neurotransmitters. CoA is often combined with choline to produce acetylcholine, a neurotransmitter with important roles in memory, attention and cognitive functions. A deficiency in pantothenic acid would include symptoms such as abdominal distress, burning sensation in the feet, fatigue, sleep disturbance and insulin sensitivity however B_5 deficiency is not common. The AI for pantothenic acid for children

aged between 9 and 13 years of age is: 5mg daily for boys and 4mg daily for girls. The UL cannot be determined at this stage, but current intakes are unlikely to be associated with adverse health effects, as there are no adverse effects of oral pantothenic acid in either humans or animals (Wellington: Ministry of Health, 2011).

Vitamin B_6 comprises six compounds: pyridoxal, pyridoxine, pyridoxamine and their respective 5' phosphates. Vitamin B_6 acts as a coenzyme in the synthesis of a number of neurotransmitters derived from amino acids including serotonin, dopamine, acetylcholine, norepinephrine and GABA. It is also required for carbohydrate metabolism and other aspects of amino acid metabolism (Mann, 2000). Clinical deficiency is rare, however symptoms can include depression, irritability and confusion (Hawkins & Barsky 1948; Leklem 1991). Hvas (2004) found that lower levels of pyridoxal phosphate were significantly correlated with higher levels of depression. Deficiency can also lead to skin problems and microcytic anaemia. The RDI of vitamin B_6 for children aged between 9 and 13 is 1mg. The UL of intake for vitamin B_6 as pyridoxine is 30mg daily for children aged between 9 and 13.

Biotin (vitamin B_7 or vitamin H) is involved in the production of amino acid proteins and fatty acids, as it is a cofactor for four carboxylase enzymes. Biotin deficiency is rare; however, it can lead to withdrawn behaviour, a delay in cognitive development or hallucinations (Gaby 2006). The evidence regarding biotin requirements was deemed insufficient to set an RDI, therefore an AI of 20µg daily for children between the ages of 9 and 13 was set. There was also insufficient evidence of adverse effects to set a UL. Preliminary research has suggested that high doses may cause weakened immune responses (Zempleni et al. 2001).

Folate (vitamin B_9) occurs naturally in a number of foods but is less stable and bio-available than its man-made counterpart folic acid. The bioavailability of folate in foods is around 50% to 60%, compared to folic acid which when used as a supplement on an empty stomach is almost 100% bio-available. Folate (or folic acid) is vital in a number of metabolic processes. Key roles include their role in the metabolism of amino acids and the production of proteins. It is also used in the manufacturing of neurotransmitters, and for the synthesis of genetic materials or DNA in cells, without folate living cells could not divide. As it is a cofactor in the synthesis of serotonin its role is vital in helping to maintain normal serotonin

levels. Depression is a common symptom of folate deficiency (Alpert, 1997). Megaloblastic anaemia and macrocytosis can also result from more severe cases of folate deficiency (Mischoulon 2000). The RDI for children aged between 9 and 13 is 300µg. The UL for dietary supplemental folic acid is not able to be established; however the UL for dietary folate is 600µg daily for children aged between 9 and 13. The LOAEL was set at 5mg daily.

Vitamin B_{12} has the biological activity of cyanocobalamin in micronutrients**.** This water soluble vitamin is required for the synthesis of fatty acids in myelin, and for the manufacturing of genetic material. Adequate intakes are also necessary for normal blood function and healthy functioning of the nervous system. Children who are deficient in B_{12} may experience growth failure. Deficiency can also lead to neurological symptoms, such as numbness, tingling of extremities, or blood related symptoms including lowered energy, shortness of breath and fatigue. Cognitive functioning can also be adversely affected from the age of adolescence (Louwman et al 2000). A major concern resulting from B_{12} deficiencies is elevated homocysteine, a possible risk factor for heart disease and Alzheimer's disease. Several studies have found that depressive patients with psychosis symptoms often had lower B_{12} levels than depressive patients with no psychosis symptoms (Bell 1991, Bell 1990). The RDI for children aged between 9 and 13 years old is 1.8µg. Vegan children would be at a high risk for vitamin B_{12} deficiency as the only natural dietary sources are in animal products. The UK Expert Group on Vitamins and Minerals (2002) states that it is not possible to establish a UL as there is insufficient data. There have been no adverse effects reported in association with excess B_{12} intake from food or supplements in healthy individuals. This apparent lack of toxicity could relate to the body's ability to decrease absorption in response to high intakes.

Choline is essential for foetal brain development and is a precursor for a number of compounds including the neurotransmitter acetylcholine. Evidence suggests that at all ages choline may improve cognitive function, learning and memory. Choline deficiency has been found to be related to poor cognitive performance (Fioravanti & Yanagi 2004). Although essential in the diet, choline deficiency appears not to occur in the general population; however, the Australia and New Zealand Ministry of Health (2006) guidelines state that consideration of choline intake needs to be further explored. The AI for children aged between nine and thirteen is 375mg daily, although animal studies suggest that females

may require less choline than males (Tessitore et al 1995). The UL for the same age group is 1,000mg daily, based on studies that reported cholinergic effects and body odour effects after large choline doses. The LOAEL was set at 7.5g daily.

Vitiamin C is water soluble and is an antioxidant necessary for normal growth and development. In humans it has been proven to protect lipids in plasma against oxidative damage (Frei 1991). It aids in the absorption of iron and copper (Hallberg 1985), the stabilisation of folate (Stokes et al 1975), and the sparing of alpha-tocopherol (Halpner et al 1998). Vitamin C is necessary for the growth and repair of tissues in all parts of the body, the body however does not naturally produce or store the vitamin. Consequently, maintaining a balance of vitamin C rich foods in the diet is important. A deficiency in vitamin C can cause scurvy, the symptoms of which can ultimately lead to death. In adults the clinical signs of scurvy begin to occur at intakes of 7-8 mg or less per day (Goldsmith 1961). The method of intake is also important. Absorption is better when, for example, 250mg is taken four times daily, rather than 1,000mg taken once daily. The RDI for children aged between 9 and 11 years of age is 40mg. The UK Expert Group on Vitamins and Minerals (2002) states that it is not possible to establish a UL for vitamin C, but sets 1,000 mg daily as a prudent limit. The LOAEL has been identified at 3,000 to 4,000 mg daily by Cameron and Campbell (1974).

Vitamin D is available in two forms, D_2 (ergocalciferol) and D_3 (cholecalciferol), both of which are used in micronutrient supplements. In the natural world, D_3 is produced by the action of sunlight on the skin, and D_2 is found in a limited range of foods. At nutritional doses these two forms of vitamin D appear equivalent; however at high doses D_2 is slightly less potent. Vitamin D_3 is preferable to D_2 as it 20-40% as effective as D_3 in maintaining serum concentrations of 25-hydroxy vitamin D. In the general population, vitamin D status is maintained through exposure to sunlight, and for this reason deficiency is more likely to occur during the winter months (Holick 1995). Vitamin D is vital to bone formation and maintenance. Research also indicates that vitamin D_3 has an important role in the functioning of the central nervous system (Garcion 2002). Abnormally low levels of vitamin D have also been found in patients with schizophrenia, depression, and alcoholism compared to healthy controls (Schneider 2000). In children, a deficiency in vitamin D can result in rickets, which leads to bowed legs and knocked knees. The AI for children aged between 9 and 13 years old 5µg vitamin D daily. Importantly, it should be taken into

consideration that children and adolescents with marginal calcium intakes may have an increased need for vitamin D (Australia and New Zealand Ministry of Health 2006). The Adult Nutrition Survey 2008/09 aimed at New Zealanders 15 years of age and above, found that around 5% of adults in New Zealand are deficient in vitamin D and a further 27% are below the recommended blood level of vitamin D (Wellington: Ministry of Health, 2011). The UL is 80µg daily for children aged nine to thirteen years, as there is little available data for children and adolescents on dose response, the UL recommendation for adults was applied.

Inositol is an isomer of glucose, which has been found to be useful in a number of psychiatric disorders, including significant benefits in the treatment of panic disorder, depression, obsessive compulsive disorder and bulimia (Gaby 2006). In one study, significant differences in levels of intracellular inositol were isolated in the brains of children with ADHD when compared to controls (Moore et al 2006). Inositol serves several important functions in the body, comprising part of all cell membranes, contributing to the function of nerves and muscles, and helping the liver process fats. The Australia and New Zealand Ministry of Health Nutrition Guidelines (2006) did not set daily dosage recommendations for inositol, and it appears that no human long-term safety studies on inositol have been conducted.

Vitamin E sourced naturally is called d-alpha-tocopherol; the synthetically produced form is dl-alpha-tocopherol. Vitamin E is a fat soluble antioxidant that helps prevent cell membrane damage. An AI dosage of α-tocopherol equivalents was set for males aged between 9 and 13 at 9mg daily. The AI dosage set for females aged between 9 and 13 years of age was 8mg daily. There have been a number of studies using supplementation of vitamin E with d- α – Tes ranging from 540mg up to 970mg a day, and other than some minor effects, adverse events have been rare. The UL for vitamin E as α-tocopherol equivalents was set at 180mg daily for children aged between 9 and 13. Larger doses above 1,000mg daily may cause bleeding problems, particularly in people taking anti-clotting medications (Sesso et al., 2008).

Vitamin K is vital for its role in blood clotting and prevention of bleeding. Deficiency can cause bleeding tendency. As a series of essential fat-soluble compounds, vitamin K is

needed for the chemical modification of a group of proteins with calcium-binding properties, consequently vitamin K contributes to maintaining healthy bones and healing fractures. The AI dosage for children aged between 9 and 13 years of age is 45µg daily. No ULs were set for vitamin K as no adverse effects have been found in animals or humans.

The following sections outline the minerals, amino acids and other ingredients found in micronutrient supplements. Presented in Table 1, are the mineral ingredients in micronutrients products and the amount of each of these minerals needed in a New Zealand child's daily diet, this is indicated in the RDI column. In Table 2, is an outline of the basic physiological or nutritional roles of other ingredients found in micronutrient supplements.

3.2.Minerals

Table 1
Micronutrient Supplement Minerals
Australia and New Zealand[1] Recommended Daily Intakes (RDI), Upper Intakes (UL), LOAEL, and Key Physiological Roles

Mineral	*RDI		**UL	LOAEL	Key Physiological Roles
	Boys	**Girls**			
Boron	Not Set	Not Set			A component in building strong bones, treating osteoarthritis and building muscle.
Calcium	1000 mg	1000 mg	2, 500 mg		Necessary for the normal development and maintenance of bones, and the proper functioning of neuromuscular and cardiac function.
Copper	1.3 mg	1.1 mg	5 mg		Deficiency results in defects in connective tissue that leads to vascular, skeletal and anaemia problems. Deficiency can also result in immune and cardiovascular problems especially in infants.
Iron	8 mg	8 mg	40 mg	70 mg	Iron deficiency is a common nutritional problem in industrialised countries, and in developing countries it is a leading cause of impairment of normal mental development of infants. Iron is an especially important component of haemoglobin which is important in transferring oxygen to tissues. It is also integral to the working of various tissues through the role it plays in enzymatic reactions. Deficiency can result in reduced physical work capacity, delayed psychomotor development in infants, impaired cognitive function and immunity, and adverse pregnancy outcomes.
Iodine	120 µg	120 µg	600 µg	1,700 µg	Required for normal growth and development of tissues, especially in the brain development of the developing foetus. Also important in energy production and oxygen consumption, therefore helping maintain the bodies metabolic rate. Iodine is also vital in the production of hormones. A recent study involving

					184 New Zealand school aged children found iodine supplementation resulted in significantly improved performance in tests of perceptual reasoning, a high level of intellectual function (Gordon et al 2009). Great progress was made in food fortification with the iodisation of salt, greatly reducing the number of countries where iodine deficiency was a public health concern. A 2006 study conducted on Australian children aged eight to ten years old, found that almost half of Australian children were iodine deficient (Li et al 2006).
Magnesium	240 mg	240 mg	350 mg	360 mg	Is a cofactor in more than 300 enzyme systems. It is involved in both aerobic and anaerobic energy generation and in glycolysis. It is also required for mitochondria to carry out oxidative phosphorylation. Magnesium plays a role in post-synaptic receptor function and has a depressive effect at synapses, inhibiting the release of neurotransmitters, such as acetylcholine, and antagonising receptors such as the NMDA receptor. Magnesium deficiency can cause depression, behaviour and personality changes, apathy, irritability and anxiety (Wacker 1968, Rasmussen 1989). An animal study involving magnesium deficiency induced in cows found deficiency to be associated with reduced dopamine levels in the cerebral cortex and cerebellum and lower noreinephrine in the corpus striatum (McCoy 2000).
Manganese	3 mg	2.5 mg	None set		Essential to the formation of bone. Is also involved in the metabolism of carbohydrates, cholesterol and amino acids.
Molybdenum	34 µg	34 µg	1, 100 µg		Acts as a cofactor for a number of enzymes.
Nickel					Nickel sensitivity can cause dermatitis and is one of the most common causes of contact dermatitis. High intakes are dangerous.
Phosphorous	1, 250 mg	1, 250 mg	4, 000 mg	NOAEL 10,000 mg daily	As phosphate is a major buffer of acid in urine and helps protect blood systemic acid balance. It also acts as a temporary store and transport mechanism for energy. Phosphorus plays a critical role in blood and extracellular fluids. Deficiency results in symptoms including anorexia, anaemia, muscle weakness, bone pain, rickets,

					confusion and muscle weakness.
Potassium	AI = 3, 000 mg	AI = 2, 500 mg	None set		A major part of intracellular fluid and a component of lean body tissues.
Selenium	50 µg	50 µg	280 µg		Functions as an antioxidant and thyroid metabolism. Selenium is used for diseases of the heart and blood vessels, including stroke and hardening of the arteries. Selenium may also help improve mood and general feelings of well-being in people with thyroiditis. Due to low soil selenium levels dietary intakes of selenium are lower in New Zealand than many other countries (Thompson 2004a). Organic selenium can almost completely be absorbed by the body, however inorganic selenium absorption is variable, generally around 50%.
Silicon	Not Set	Not Set			Orthosilicic acid is the form predominantly absorbed. Deficiency induces deformities in skull and peripheral bones, poorly formed joints, reduced contents of cartilage, collagen, and disruption of mineral balance in the femur and vertebrae (Martin 2007).
Sulphur	Not Set	Not Set			Is a key constituent of numerous nutrients including biotin and thiamin. Cysteine and methionine, two of the body's sulphur containing amino acids, have powerful antioxidant properties and help control the absorption of heavy metals, such as lead.
Vanadium	Not Set	Not Set			Vanadium's primary mode of action is as a cofactor that enhances or inhibits enzymes. It has potential to play a role in the building material of bones and teeth, and in the treatment of diabetes (Badmaev et al 1999). Before it can be helpful in pharmacological doses the gastro side effects from of vanadium must be reduced.
Zinc	6 mg	6 mg	25 mg	60 mg	Helps maintain the structural integrity of proteins and regulate gene expression. Mild deficiency can lead to impaired growth velocity, suboptimal pregnancy outcomes and impaired immune responses. Severe deficiency can also result in alopecia, diarrhoea, delayed sexual development and impotency, eye and skin lesions and impaired appetite. Psychological consequences of zinc deficiency include behavioural disturbances, depression and

					mental confusion (Mann, 2000). Lower zinc levels have been found to correlate with increased depression severity within major depression populations (Maes 1994).

Notes:
***Based on a child aged between 9-11 years old or 9- 13 years old.**
**** Based on children and adolescents aged between 9 – 13 years old.**
[1] **NHMRC. (2006).** ***Nutrient reference Values for Australia and New Zealand including Recommended Dietary Intakes.*** **Canberra, Australia.**

3.3. Other vitamins and amino acids

Table 2
Other Micronutrient Supplement Ingredients

Ingredient	**Key Physiological/Nutritional Roles**
Betanine	Natural Dye
Saccharin	Artificial sweetener
Sodium Cyclamate	Artificial sweetener banned in the U.S.
Sodium Bicarbonate	Can be used as an antacid
Sodium	An essential nutrient that regulates blood volume, blood pressure, osmotic equilibrium and pH.
Spirulina	A complete protein containing all essential amino acids. It also contains in very small amounts vitamins B_1, B_2 , B_3, B_6, B_9, vitamin C, vitamin D, vitamin A and vitamin E. It is also a source of potassium, calcium, chromium, copper, iron, magnesium, manganese, phosphorus, selenium, sodium and zinc.
Taurine	An amino acid that supports neurological development and helps regulate the level of water and mineral salts in the blood. It is also thought to have antioxidant properties.
Lecithin	Lecithin is a lipid that consists mostly of choline. It helps to prevent arteriosclerosis, protects against cardiovascular disease, improves brain function, helps keep the liver and kidneys healthy, aids in thiamin and vitamin A absorption.
Isomalt	Natural sugar substitute
Ashwagandha root	Helps to boost the immune system and alleviate stress. The herb is also used to treat inflammation, improve memory and provides a rich source of antioxidants.
Burdock root	The beneficial effects of this herb include increasing circulation to the skin, helping to detoxify the epidermal tissues.
Astragalus root	Contains antioxidants. It is used to protect and support the immune system, and has anti-inflammatory properties.
Sarsaparilla root	A few reports suggest that sarsaparilla has both anti-inflammatory and liver-protecting effects.
Fennel seed	This herb is rich in potassium - an essential mineral. It is also useful for treating bloating.
Ginko leaf	Has been shown to be moderately effective in improving cognition in dementia patients. Also the treatment of the effects of mild to moderate cerebrovascular insufficiency as well as the effects of peripheral arterial occlusive diseases.

Gotu kola leaf	Small herbal plant. Thought to aid wound healing. A mild adaptogen.
Gymnema sylvestre leaf	Thought to help in the treatment of diabetes.
Milk thistle seed	Supports optimal liver function.
Schisandra fruit	Is used for treating liver disease (hepatitis) and protecting the liver from poisons. Is also used as an adaptogen for increasing resistance to disease and stress.
Slippery elm bark	Contains antioxidants that help relieve inflammatory bowel conditions. Slippery elm also causes reflux stimulation of nerve endings in the gastrointestinal tract leading to increased mucus secretion. The increased mucus production may protect the gastrointestinal tract against ulcers and excess acidity.
Mannitol	May be useful clinically both as a diuretic and as an obligate extracellular solute.
Lactobacillus acidophilus	When included with a blend of other bacteria strains decreased the incidence of paediatric diarrhoea. It has been shown to improve bowel regularity.
Rose Hips	Contain a lot of vitamin C when fresh, but this is decreased substantially when dried and processed. Rose hips are also used for treating symptoms of stomach disorders.
Fructose	Fruit sugar found in many plants.
Sugar Alcohol	Hydrogenated form of carbohydrate, often used in place of sucrose.
Sugar/ sucrose /glucose	Sweetener
Dextrose	Glucose
Tapioca Syrup	Natural Sweetener
Citric Acid	Weak organic acid
Malic Acid	Known for its ability to increase energy and tolerance to exercise. This is because it is an essential component in the Krebs cycle, which is how our bodies convert food into energy.
Vegetable Cellulose	The dietary fibre that cellulose provides helps prevent constipation.
Xanthan Gum	Food additive
Silica	A mined mineral used as a flow agent and as a source of silicon.
Vegetable Magnesium Stearate	Its lubricating properties allow powders to flow freely through encapsulation machines without sticking.
Vegetable Stearic Acid	Often used as a filler in the manufacturing of drug or dietary supplement capsules.
Corn Starch	Thickening agent
Carrageenan	A family of linear sulfated polysaccharides that are extracted from red seaweeds. Studies suggest it might function as a topical microbicide.

Propylene Glycol Alginate	An emulsifier, stabilizer, and thickener used in food products.
Luo Han Guo fruit extract	Natural sweetener
Vegetable Stearin	A wax derived from vegetable sources used as a lubricant in tablet compressing.
Saccharides	Sugars
Acesulfame K	Sweetener
Strawberry Powder	An antioxidant.
Pectin	Used as a gelling agent, thickening agent and stabilizer in food.
Sodium Citrate	A sodium salt that occurs naturally in the body. It is known as a buffer, meaning it can absorb hydrogen ions from acids and prevent large changes in the pH of solutions. This buffering capacity can help food and solutions remain stable over time. Additionally, buffers, such as sodium citrate, play critical roles in maintaining proper physiological conditions in body fluids, such as blood.
Sunflower Oil	High in vitamin E and low in saturated fat.
Cane Juice	Natural Sugar
Tableting Aids	A food grade substance that is added to a dietary supplement to constitute the form in which that supplement is sold; and includes an encapsulating aid.
Carnauba wax	Plant derived coating.
Mangosteen Fruit	Rich in antioxidants
Cranberry fruit	Raw cranberries have moderate levels of vitamin C, dietary fibre and manganese. Are of possible benefit to the cardiovascular system and immune system
Broccoli	Includes vitamin C, vitamin A (mostly as beta-carotene), folic acid, calcium, and fibre.
Spinach	Contains vitamin K and vitamin A, manganese, folate, magnesium and provides dietary fibre.
Asparagus Stems	Has a good level of dietary fibre. Fresh asparagus are rich in folates. Fresh asparagus also contains fair amounts of anti-oxidant vitamins such as vitamin-C, vitamin-A and vitamin-E and vitamin K.
Carrot Root	Are an exceptionally rich source of carotenes and vitamin-A. Beta carotene is one of the powerful natural anti-oxidant helps protect body from harmful fee radical injury. In addition, it also has all the functions of vitamin A such as vision, reproduction (sperm production), maintenance of epithelial integrity, growth and development.
Tomato Fruit	Contains Lycopene. Lycopene is a vital anti-oxidant that helps in the fight against cancerous

	cell formation as well as other kinds of health complications and diseases.
Acai Fruit	Contains calcium, vitamin A, aspartic acid and glutamic acid.
Pomegranate Fruit	High in vitamin C and polyphenols, both substances which act as antioxidants and are naturally high in fibre.
Grape seed	Contains protein, lipids, carbohydrates and polyphenols. Acts as an antioxidant.
Germanium Sequioxide	There are two general forms of germanium: organogermanium compounds, which are carbon-containing compounds and inorganic geranium. This may have an anticancer effect.
Alpha lipoic Acid	Is one of the good fatty acids produced in every one of our cells. It is also an antioxidant.
Glutathione	Is a potent antioxidant.
Garlic extract	Garlic has been found to enhance thiamin absorption. Garlic is also a vasodilator.
Lactoferrin	Is a multifunctional protein, and one of the components of the immune system of the body
Silymarin	Is derived from milk thistle. Proved to be successful in treating alcohol-related liver disease.
Royal bee jelly	Is a source of biopterin
Bilberry extract	Is beneficial for eye health.
Soy constituents	Can lower plasma levels of low-density lipoprotein (LDL) and cholesterol.
Dandelion	The scientific name is taraxacum officinale. It is used as a diuretic, a mild appetite stimulant and to improve upset stomach.
Echinacea	Supports the immune system.
Pineapple Fruit	Is a rich source of soluble and insoluble dietary fibre such as pectin.
Apple Fruit	Rich in dietary fibre. It contains good quantities of vitamin C and beta-carotene. They are also are rich in antioxidant phyto-nutrients flavonoids and polyphenols.

3.4. Nutrients Summary

There are a large number of ingredients included in micronutrient supplements. These ingredients play a wide variety of roles. Some of these ingredients appear to be included in supplements to ease pill consumption, to aid in the binding of supplement ingredients, to act as a sweetener, or to flavour the supplement. Other ingredients may play a number of mental or physical health roles. The combination of these ingredients may lead to varied or additive effects, not seen when nutrients are given on their own.

4. The New Zealand Context

In 2006, a nationally representative sample of the New Zealand population completed the New Zealand Mental Health survey (Oakley-Browne, Wells and Scott, 2006). The prevalence of any mental health disorders in the previous 12 months in young people between the ages of 16 and 24 identified by this survey was 28.6% (95% CI: 25.1, 32.3). The prevalence of a serious disorder for this population was 7.2% (95% CI: 5.7, 9.0). For both male and female New Zealanders the rates of depression have been found to be increasing with each birth cohort and the age of onset is lowering (Joyce et al. 1990). The importance of finding the most effective treatments increases with the increasing mental health prevalence represented in the New Zealand population and in particular with the decreasing age of disorder onset. In New Zealand, the highest prevalence of any mental health disorder is in Maori and Pacific people when compared with any other ethnic group (Oakley-Browne et al., 2006). Disorder prevalence's are also higher for people who are disadvantaged either in education or household income (Oakley-Browne et al., 2006).

There is an indication that New Zealand children attending primary or secondary medical care have a high useage of complementary and alternative medicine (CAM). In a sample of 100 Christchurch children in primary or secondary medical care under the age of 12, Wilson, Dowson and Mangin (2007) found that the overall CAM-use was 70%. This prevalence rate is higher than that found in similar populations in Australia and Wales where prevalence was reported at 51% (Nicholson, 2006) and 41% (Armishaw & Grant, 1999) in Australia and Wales respectively. Of note, was that the children and parents in the Wilson, Dowson and Mangin (2007) survey were largely of New Zealand European ethnicity (87% and 90% respectively) and therefore may not be representative of all regional populations in New Zealand.

Participants reported the use of 35 different CAM types. The two most common CAM treatments were arnica (43%) and multivitamins (17%). It was reported by the parents that CAM was predominantly as used for the prevention and treatment of acute or short-term symptoms. A valuable predictor of CAM use was found to be parents who use CAM treatments themselves. Children of parents who use CAM were found to be four times more likely to use CAM than those children whose parents do not use CAM. Higher education of the participating parent was also found to be strongly correlated with child CAM use. The results found by Wilson, et al. (2007) suggest that a large number of New Zealand parents use a variety of types of CAM in order to prevent or treat short term illnesses in their child receiving primary or secondary medical care. The higher rate of use among this Christchurch sample compared to the use in other countries could

mean that overall use of CAM in New Zealand children is higher. It may also indicate that micronutrient use is higher than international prevalence rates. The prevalence use of micronutrients will be explored in this research's survey.

5. The Current Investigation: Aims and Hypotheses

It is the aim of this study to investigate whether the micronutrient supplements found to be effective in research, have ingredients or dosages comparable to micronutrients for children that are available over the counter. The ingredients and dosages for micronutrient supplements used in psychologically based studies that focus on children, will be found in a literature search of papers published internationally. The ingredients and dosage's used in commercial products will be found from a broad array of micronutrient supplement brands available over the counter in New Zealand. The commercial micronutrient sample will be drawn from New Zealand supermarkets, health food stores and pharmacies, and a small sample will be included from supplements available over the counter in the U.S., Australia and England. It may be helpful to both consumers and practitioners to identify one or more New Zealand in-store micronutrient supplement that fits the effective research dosage and ingredient parameters. The comparison of the commercial and research micronutrient supplements may provide information to micronutrient users as to the likely efficacy of the in-store products on the psychological, cognitive and mood symptoms of their child.

The aim of the on-line survey is to identify the key motivations of New Zealand parents when purchasing a micronutrient supplement for their child. In the survey the use of micronutrients given to New Zealand children is explored through questions that investigate: the most popular NZ micronutrient brands, demographic information about the parent, whether parents follow the recommended dosage when giving the supplement to their child, whether parents give any other dietary supplements to their child, parent's strongest motivating factors in purchasing a micronutrient supplement for their child, the factors that influence their choice of micronutrient brand, and any perceived benefits that the parent attributes to micronutrient use. It is hypothesised that New Zealand parents will not be aware of the benefits of micronutrients for psychological symptoms, cognition and mood, and consequently will not purchase micronutrients for these purposes.

Method

1. Study 1: Micronutrient Supplement Investigation

1.1. Micronutrient Products

A micronutrient supplement was defined as any product that labelled itself as a 'multi-nutrient, multivitamin and, or, multi-mineral, or micronutrient supplement' and included three or more vitamins and/or minerals and/or amino acids. Research products were defined as a micronutrient supplement tested on children and used in a psychologically focussed, micronutrient study. The products EMPowerplus and Spectrum Support are high end products available to purchase direct from the supplier on the internet. These products however, were classified as research products as they have both been tested in micronutrient research and cannot be brought in stores or from on-line pharmacies. Commercial products selected for comparison included at least one micronutrient product for children from each of the micronutrient brands that were available in New Zealand at the time of the search (December 2011). The commercial products were found over the counter in supermarkets, health stores, and pharmacies, and on New Zealand based pharmaceutical internet sites. The commercial products also include a random selection of micronutrient supplements for children, that are available over the counter or on pharmaceutical internet sites based in Australia, America and the United Kingdom.

In order to identify the average micronutrient composition of an effective supplement the papers included in the ingredient analysis were limited to those that found a significant effect in symptom reduction following micronutrient treatment. There were two papers that fit this criterion that were not included in the analysis as the ingredients and dosages of the supplements used were not supplied. The first of these two papers was Katz et al. (2010) which found a significant improvement in ADHD symptoms following broad base micronutrient supplement administration. The second of these papers was Weeks (2004), who found significant reductions in the abnormal characteristics of downs syndrome following supplementation. A further three papers which are outlined in Table 3, were not included in the analysis as they did not find significant symptom reductions as a result of micronutrient supplementation. Two of the three papers provided their ingredients and dosages; these were Sinn and Bryan (2007) and Nelson, et al. (1990). The third paper that did not find a significant effect was Perlman, et al. (2010). Perlman,

et al. (2010) did not provide the ingredients or dosages of the supplement administered to participants in the research paper or upon request; however, the supplement was described by the author as equivalent to over the counter multivitamins.

Table 3
Studies that Did Not Find a Significant Symptom Reduction.

Micronutrient Supplement	**Psychological Area Explored**	**Researcher's Postulated Reason for Non-significant Result**
Sinn & Bryan (2007)	Attention Deficit Hyperactivity Disorder (ADHD) symptoms	Dosages too low for a clinical sample.
Nelson et al. (1997)	Intelligence Quotient (IQ)	Trial period to short.
Perlman et al. (2010)	Academic Achievement	Micronutrient composition possibly in-effective.

The ingredients and dosages of the research and commercial micronutrients were recorded in one table under the headings: vitamins, minerals, amino acids, polyunsaturated fatty acids, and other ingredients, an excerpt from the full table can be seen in Appendix C. For each micronutrient supplement, both the dose and largest recommended daily dose was recorded. The amount of each nutrient at the largest daily recommended dosage for a child was then calculated. When recommended dosages were based on age, the dosage was calculated for the age bracket between eight and thirteen years of age. When the recommended dosage was weight based, the weight bracket less than or equal to 100 pounds was calculated. Once completed, the table contained 13 different effective research micronutrients supplements (see Table 4), and 22 commercial micronutrients supplements (see Table 5). The number of times each vitamin or mineral occurred across the 13 research supplements was then calculated. The same process was then repeated for the 22 commercial products. This calculation allowed the comparison of the frequency with which a vitamin or mineral appeared in research supplements compared to commercial supplements. The dosage of each ingredient was then normalised to either micrograms (µg) or milligrams (mg). This normalisation was done to allow for ease of comparison across the supplements. For example, using the 30% International Unit conversion rate for vitamin A (retinol), 1 International Unit (IU) of vitamin A was re-recorded at 0.3 µg.

Table 4
Effective Research Micronutrients and the Psychological Areas Explored

Micronutrient Supplement*	Psychological Area Explored
1. Kumar M, & Rajagopalan S. 2008	Intelligence Quotient (IQ)
2. Sandstead, H. et al., 1998	Intelligence Quotient (IQ)
3. Osendarp, S. et al., 2007	Intelligence Quotient (IQ)
4. Harrell R. et al., 1981	Down Syndrome Symptoms
5. Xia, R. 2011	Autistic Spectrum Disorders (ASD)
6. Schoenthaler et al., 2000	Intelligence Quotient (IQ)
7. Harding et al., 2003	Attention Deficit Hyperactivity Disorder (ADHD)
8. Adams et al., 2011	Autistic Spectrum Disorders (ASD)
9. Klaire Laboratory Supplements	Mood and General Behaviour Intelligence Quotient (IQ)
10. Larkhall Laboratories	Intelligence Quotient (IQ)
11. Spectrum Support Vitamins & Minerals III	Autistic Spectrum Disorders (ASD)
12. EMPower Plus (including and after 2009)	Paediatric Bipolar Disorder
13. EMPower Plus (pre 2009)	Mood and General Behaviour

*Notes: *Researchers are named as the micronutrient supplement when the supplement did not have its own name or was not given a name (i.e. was specifically created for the experiment).*

Table 5
Commercial Micronutrients

1. Healtheries Fizz Bomb
2. Healtheries Kidscare Chewables
3. Healtheries Tongue Fizzer
4. Blackmores Kid's Multivitamin
5. Centrum Kids Complete
6. Nature's Own Child Care Multivitamin & Mineral
7. Nature's Sunshine Heroes Multiple Vitamin & Mineral
8. Thompsons Animals Jnr Immunofort
9. Radiance Kids Multivitamin
10. Solgar Kangavites Complete Multivitamins & Minerals
11. Emergen-C Kids Multi-Vitamin Fizzy Drink Mix
12. Iceberg Labs KIDZ Multivitamins
13. Rainbow Light Essential Gummies Multivitamin & Multimineral
14. Essentials Children's Multi with Acidophilus
15. Healtheries Teen Multi
16. Flinstones Gummies Complete (Bayer)
17. Children's Probiotic & Multivitamins (Lloyds pharmacy)
18. Kindervital Tonic (Floradix)
19. Every Day Please (Microgenics)
20. Yummi Bears Multi-Vitamin & Mineral (Hero Nutritionals)
21. Kordel's DHA Smart Multi
22. Nature's Plus Animal Parade Chewable

1.2. Active Compound Identification

The micronutrient ingredients in the supplements were listed in a number of different forms for each vitamin or mineral. For example, vitamin C was listed in four different forms: ascorbic acid, sodium ascorbate, calcium ascorbate and mixed mineral ascorbates. To enable equitable comparison across the micronutrient supplements, the dose amount of the active compound in each of the different forms was calculated. The calculations for finding the active component of vitamin C in each of its given forms can be seen in Table 6.

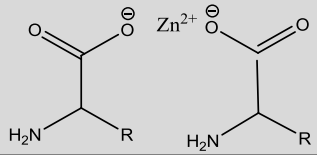
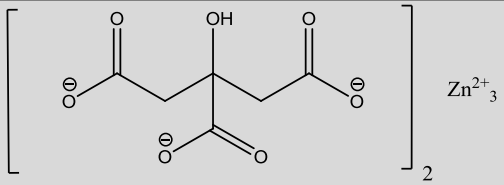
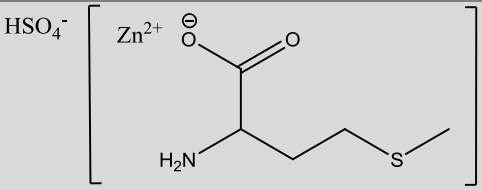
The active compound dose was not calculated for all of the nutrients. Vitamins were selected for the conversion based on their previously documented role in psychological functioning. The active compound dosage was calculated for vitamins: A, B_1, B_2, B_3, B_5, B_6, B_7 (biotin), B_9 (folic acid), B_{12}, C, and D. The active compound dosage was not calculated for the minerals due to the complexity of identifying the correct chemical formula used in each mineral variation. This is highlighted in Table 7, where as an example, the percentage of zinc was

calculated for the six different forms of zinc used across the micronutrient supplements. Table 7 indicates the difficulty in assuming the correct chemical formula, and therefore the zinc component of these mineral compounds. Different commercial suppliers of these minerals have varying chemical formulas, therefore only the average zinc component loading for these minerals could be presented.

Table 6
Calculations for finding Vitamin C (Ascorbic Acid) Component

Vitamin C Form	Rate of Conversion	Calculation	Vitamin C Component
Sodium Ascorbate	Ascorbic acid= 88.9% of sodium ascorbate	120mg x 88.9%	106.68 mg
Calcium Ascorbate	Ascorbic acid = 89.85% of calcium ascorbate	900mg x 89.8%	808.2 mg
Mixed Mineral Ascorbate	Ascorbic acid = approximately 88% of mixed mineral ascorbates	500mg x 88%	440 mg

Table 7
Zinc Active Component Calculations

Zinc Compound	Chemical Formula	Approximate Percentage of Zinc Present
1. Zinc Oxide	ZnO	80 %
2. Zinc Amino Acid Chelate		* 10 %
3. Zinc Citrate		34 %
34 Zinc chelate	* Based on EDTA (Ethylenediaminetetraacetic acid)	* 12 %
35 Zinc Monomethionate		Not known
36 Zinc Sulfate	$ZnSO_4$	40 %

*Notes: * As indicated by common commercial product loadings of zinc component.*

1.3. Data Treatment

Data analysis was carried out with the aim of identifying the vitamin dose properties across the studies that found a significant effect. Eighteen studies that provided their supplement ingredients fit this criterion, seen in Table 4. Each of the research supplement vitamins were converted to their active compound, and following this the median, maximum and minimum daily dose was calculated. In order to provide the most accurate picture of the data, the median was chosen as the measure of central tendency. This choice was made due to top end outliers. These outliers are reflected in the maximum values of the affected vitamins. The median vitamin dose in research supplements is the median dose found to have a psychological effect in a micronutrient supplement. This dose was calculated by ordering the doses from each study that found a significant effect and identifying the median dose value. The median, maximum and minimum dose calculations were then carried out on the commercial micronutrient vitamins. The final step, was the use of the non-parametric, two-tailed Mann-Whitney test, to identify whether the mean daily dosages of the research and commercial supplements were significantly different.

2. Study 2: Why Do New Zealand Parents Give their Children Micronutrients?

2.1. Participants

Participants needed to be over 16 years of age, currently living in New Zealand and have at least one child under the age of eighteen residing in their household (did not have to be a biological child). Three hundred and sixty five parents participated in the survey. Of these participants, 95% were female and 5% were male. Eighty eight percent of participants were New Zealand European. The ethnicities of the remaining participants were as follows: 6% other European, 5% Maori, 1% Chinese. Participants in this sample were from a range of cities in New Zealand including: Auckland, Christchurch, Wellington, Dunedin, Hokitika, Taranaki, Taupo, Hastings, Oamaru, Waikato, Tauranga, Palmerston North and New Plymouth. The most common categories for employment status of participants was: trained service worker 20% (i.e. police, nurse), at home parent 32%, clerical or sales 9%, self-employed 7%, business manager or executive 5%, professional worker 8% (i.e. lawyer, doctor) and manual worker 5%.

2.2. Procedure

Participants were recruited via social networking advertisement. Advertisements were placed on multiple New Zealand based parenting websites (Kiwi Families, Parents Centre and the Parenting Place); the community thread on Trade Me, and were circulated via company emails

(The Press and Couplands). All advertisements displayed a website address that enabled participant's access to the web-based survey. Once participants completed the survey they were offered the opportunity to enter a draw to win one of three $100 supermarket vouchers as a thank you for their time. Any information participants provided when entering the voucher draw, could not be linked to their survey responses, ensuring participants the anonymity of their responses.

2.3. The Survey

The web-based survey programme used to create the questionnaire was Qualtrics. Before completing the survey, respondents were directed to a web page with information regarding the question content of the study, the study's purpose, and contact details of the primary researchers, as can be seen in Appendix A. This information page concluded by informing participants that any personal information given in the questionnaire could in no way be associated with their name, computer log-in or any other identifiable information. This information page also requested responders to give their informed consent to participate. Participants were informed that they could withdraw from the survey at any point without consequence.

The number of survey questions was dependant on whether or not the respondent gave their child a micronutrient supplement. Respondents who indicated they purchase a micronutrient supplement for their child were asked to answer 19 questions, and those that did not purchase a micronutrient supplement were asked 12 questions, in both cases not all questions were mandatory. The survey took around five minutes to complete and is presented in Appendix B. The questions covered demographics, personal background, their child's mental and physical health, and a number of factors based around their purchasing and administering of micronutrients (see Appendix B). The micronutrient based questions included: do any of the children in your household take any other type of supplement; for approximately how long have they taken a multivitamin; do they generally take the recommended dosage of multivitamin; for what reasons do you buy your child a multivitamin; what brand of multivitamin do you most often purchase; is there anything specific you look for in the ingredients; what factors are most influential in your choice of multivitamin; have you perceived any benefits from your child taking a multivitamin. All responses were obtained between April 16th and May 25th (2012). Respondents were again given the primary researchers details should they have any questions, or wish to further discuss any issues raised in the survey.

Results

The results are presented separately for the micronutrient product and the survey investigation. Firstly, the frequency with which each vitamin or mineral appeared in research and commercial supplements is presented, followed by the descriptive statistics for each vitamin. The non-parametric comparison of the research and commercial dosages are presented. Following this is the descriptive statistics of each vitamin, including a graphical representation of the dosages across research and commercial supplements. Lastly, is an explanation for the removal of outliers from the dose sets. This reasoning is presented in both descriptive statistics and graphical form.

1. Study 1: Micronutrient Product Investigation

The vitamin and mineral ingredients in the research and commercial supplements did not differ greatly. For example, thiamin appeared in 78% of the effective research supplements, and 86% of the commercial supplements (seen in Table 8). Zinc also featured at a similar frequency in the research and commercial supplements: 77% of the research supplements and 82% of the commercial supplements (seen in Table 9). Out of all the vitamins and minerals, one ingredient was included in all of the supplements, this ingredient was pyridoxine.

Table 8
The Frequency of Vitamin Inclusion in Each of the Micronutrient Supplements included in the Data Analysis

Vitamin	**Percentage of Effective Research Supplements vitamin included in**	**Percentage of Commercial Supplements vitamin included in**
Vitamin A	78%	95%
Thiamin (B_1)	78%	86%
Riboflavin (B_2)	78%	82%
Niacin (B_3)	85%	91%
Pantothenic Acid (B_5)	78%	95%
Pyridoxine (B_6)	100%	100%
Biotin (B_7)	46%	77%
Folic Acid (B_9)	78%	86%
Cyanocobalamin (B_{12})	92%	100%
Vitamin C	78%	100%
Vitamin D	78%	91%
Vitamin E	78%	95%
Vitamin K	23%	14%
Choline	54%	41%
Inositol	54%	36%

Notes: - Percentages are rounded to the nearest whole number.
- In some cases supplements included multiple variations of the same vitamin. This is not represented in this data.
- The research supplement percentages are based on the ingredients of effective micronutrient supplements that provided their ingredient and dose information.

Table 9
The Frequency of Mineral Inclusion in Each of the Micronutrient Supplements included in the Data Analysis

Mineral	**Percentage of Effective Research Supplements mineral included in**	**Percentage of Commercial Supplements mineral included in**
Boron	23%	0%
Calcium	69%	86%
Chromium	69%	27%
Copper	46%	27%
Iron	69%	63%
Iodine	54%	68%
Fluoride	7%	0%
Magnesium	69%	73%
Manganese	77%	56%
Molybdenum	69%	9%
Nickel	15%	0%
Phosphorus	23%	14%
Potassium	46%	50%
Selenium	62%	23%
Silicon	7%	0%
Sulphur	15%	0%
Vanadium	23%	0%
Zinc	77%	82%

Notes: - Percentages are rounded to the nearest whole number.

- In some cases supplements included multiple variations of the same vitamin. This is not represented in this data.
- The research supplement percentages are based on the ingredients of effective micronutrient supplements that provided their ingredient and dose information.

1.1. B Vitamins

The Table 10 displays the daily dose median and range for each B vitamin. The results indicate that research supplement B vitamin doses are higher than doses in commercial supplements. Table 10 also shows an overall broader dose range in the research supplements when compared to commercial supplements.

Table 10
B Vitamin Median Daily Dose and Dose Distribution Properties in Research and Commercial Micronutrients

Vitamin	Research Supplement Median (SD)	Commercial Supplement Median (SD)	Research Supplement Minimum-Maximum Dose	Commercial Supplement Minimum-Maximum Dose
Thiamin (B_1)	14.59 mg (11.52)	1.22 mg (0.89)	0.7 – 243.18	0.6 – 40.84
Riboflavin (B_2)	13.5 mg (12.84)	1.7 mg (2.11)	0.85 - 200	0.55 - 10
Niacin (B_3)	63.75 mg (36.87)	13.5 mg (5.43)	10 - 750	2.5 - 20
Pantothenic Acid (B_5)	22.08 mg (54.76)	7.5 mg (2.56)	0.92 – 450.8	1.5 - 10
Pyridoxine (B_6)	23.04 mg (18.87)	1.78 mg (1.61)	0.9 – 287.95	0.7 – 8.23
Biotin (B_7)	400 µg (429.31)	50 µg (90.65)	10 - 150	10 - 1000
Folic Acid (B_9)	560 µg (703.48)	100 µg (132.52)	35 – 2048.5	5 - 400
Cyanocobalamin (B_{12})	900 µg (490.71)	5 µg (2.04)	1 - 500	0.64 - 750

As the data did not follow a normal distribution, a two-tailed Mann-Whitney test was conducted for each vitamin. The Mann-Whitney test was used to evaluate if the research and commercial supplements had significantly different daily doses. The results of all tests were in the expected direction, whereby the research supplement dose was larger than the commercial supplement dose. The effect size was calculated for each Mann-Whitney test, this was calculated using N (total number of supplements) and the Z score. The standard value of *r* for a small effect size is 0.1, 0.3 for a medium effect size and 0.5 for a large effect size. Outliers were removed before conducting non-parametric tests and dose distribution graphs. These extreme scores were removed to improve the test accuracy and reduce the errors of inference (Osborne and Overbay, 2004). For each vitamin, no more than one outlier was removed from each of the supplement categories.

The median thiamin daily dose for research and commercial supplements was 14.59mg and 1.22mg respectively. The maximum research dose was 243.18mg and the maximum commercial dose was 40.84mg. Mann-Whitney test results indicated that the research and commercial supplements differed significantly from each other, $U(29) = 36.5$, $p < .01$, $r = .55$ (*see* Table 11). This

difference is clearly highlighted in Figure 1 which shows the dose distribution across both research and commercial supplements, with research doses on the left side of the graph and commercial doses on the right.

Thiamin Daily Dose (mg):

Research versus Commercial Supplements

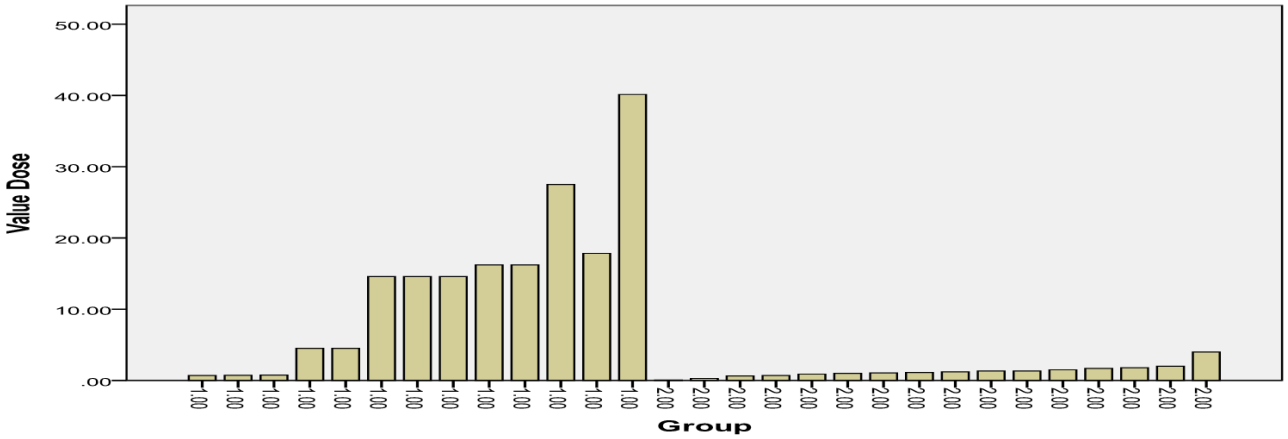


Figure 1. Thiamin Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The median riboflavin daily dose was 13.5mg in the research supplements and 1.7mg in the commercial supplements. Test results show that the research riboflavin daily dose was significantly higher when compared to the commercial riboflavin dose, (U (32)= 62.5, $p < .05$, $r = .43$, see Figure 2).

Riboflavin Daily Dose (mg):

Research versus Commercial Supplements

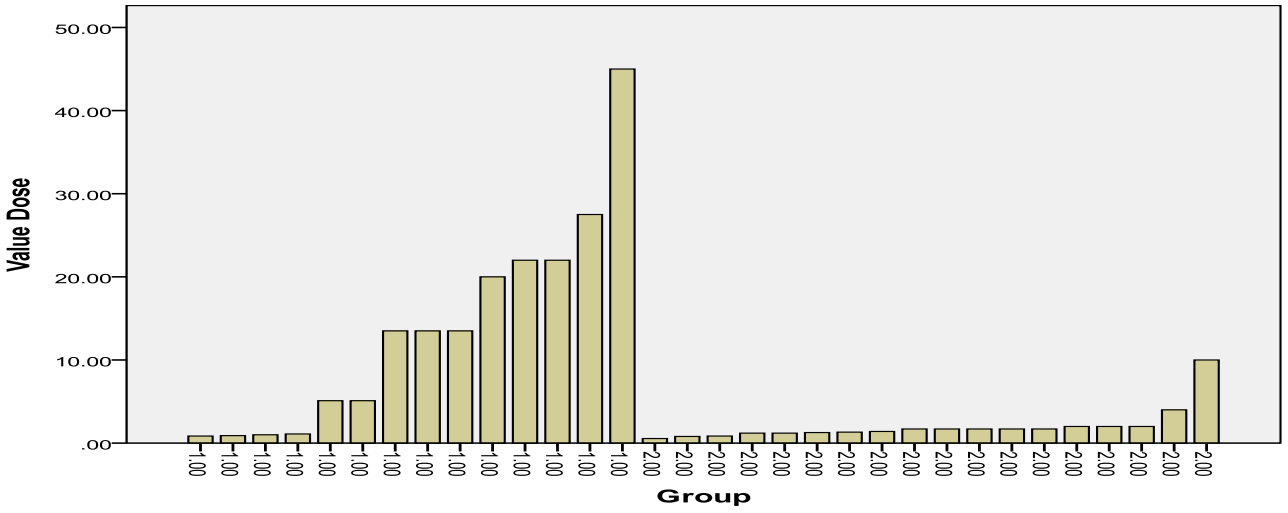


Figure 2. Riboflavin Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The niacin median daily dose in research and commercial supplements was 63.75mg and 13.5mg respectively. The research and commercial niacin doses were found to be significantly different U (32)= 41.5, $p < .05$, $r = .56$. This significant group difference is highlighted in Figure 3, as the research daily doses of niacin are clearly overall larger than the commercial doses.

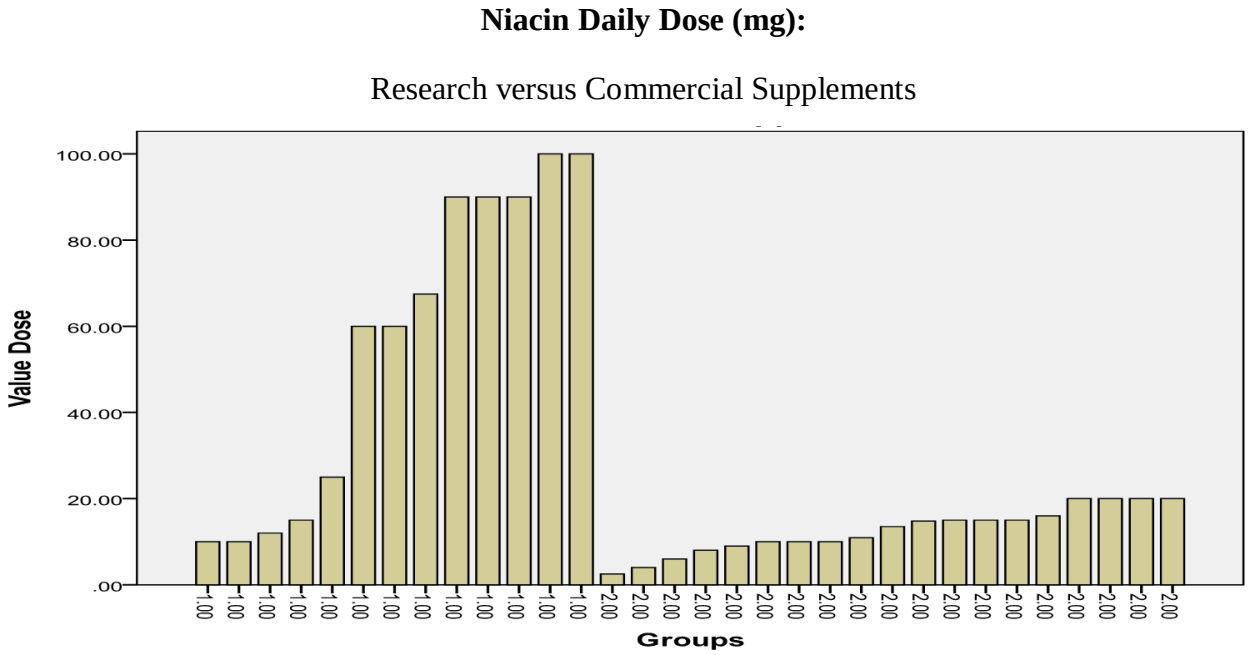


Figure 3. Niacin Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

Table 11

Nonparametric test of group difference in Daily Dose Between Research and Commercial Micronutrient Supplements.

Vitamin	U (Mann-Whitney)	Z	N (Total Number)	Significance (2 tailed)	r (Effect Size)
Thiamin (B_1)	36.5	-2.96	29	.003	.55
Riboflavin (B_2)	62.5*	-2.42	32	0.16	.43
Niacin (B_3)	41.5	3.16	32	0.002	.56
Pantothenic Acid (B_5)	21	-3.95	33	0.000	.69
Pyridoxine (B_6)	79	-2.88	38	0.004	.47
Biotin (B_7)	26	-3.08	27	0.002	.59
Folic Acid (B_9)	44.5	-3.25	33	0.001	.57
Cyanocobalamin (B_{12})	75	-2.68	36	0.007	.45
Vitamin A	120 *	-1.06	35	0.289	.18
Vitamin C	56.5	-3.06	35	0.002	.52
Vitamin D	74.5	-2.19	33	0.029	.38

Note: * *U* values are not significant.

*Small effect size 0.*1, medium effect size 0.3, large effect size 0.5.

The research median dose was also higher than the commercial supplement median for pantothenic acid (research Mdn 22.08mg, commercial Mdn 7.5 mg, see Table 11). The pantothenic acid dose in research supplements was significantly higher than the commercial supplements dose, *U(33)* = 21, $p < .001$, $r = .69$, which can be clearly seen in the dose distribution in Figure 4.

Pantothenic Acid Daily Dose (mg):

Research versus Commercial Supplements

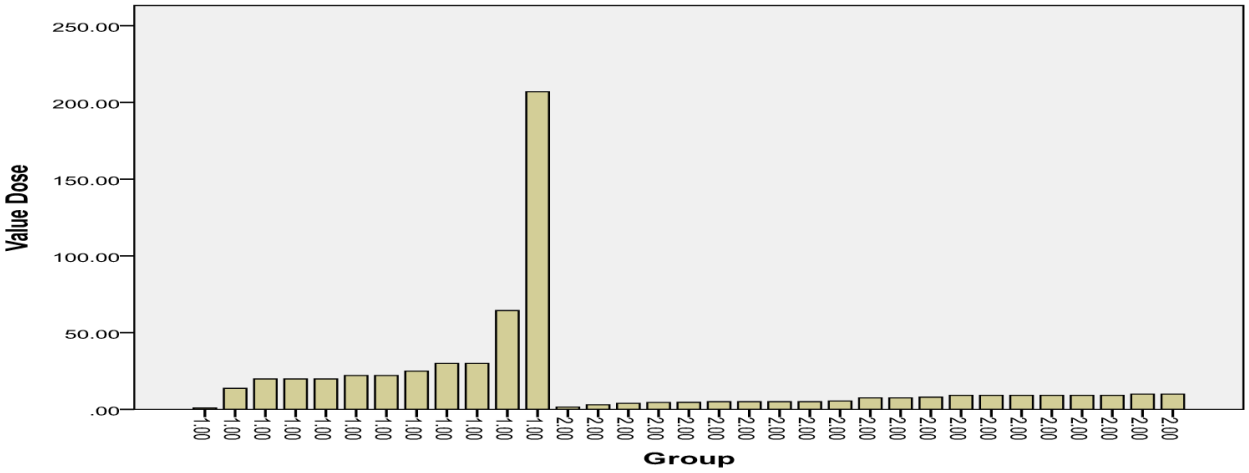


Figure 4. Pantothenic Acid Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The research median daily dose for pyridoxine was 23.04mg, in contrast to the commercial median of 1.78mg. The difference between the research and commercial daily doses of pyridoxine was found to be significant, U (38)= 79, p <.01, r = .47. This significant dose difference is highlighted in Figure 5.

Pantothenic Acid Daily Dose (µg):

Research versus Commercial Supplements

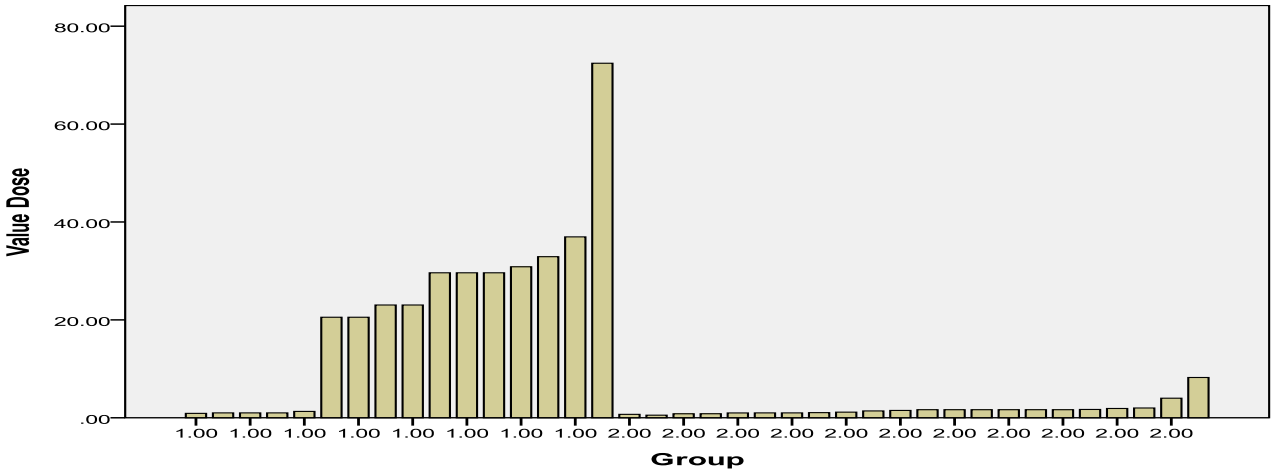


Figure 5. Pantothenic Acid Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The research and commercial biotin dose medians were 300µg and 50µg, respectively. The biotin daily dose was found to be significantly different in the research compared to the commercial

supplements as can be seen in Figure 6, (*U(27)* = 26, *p* <.01*, r* = .59).

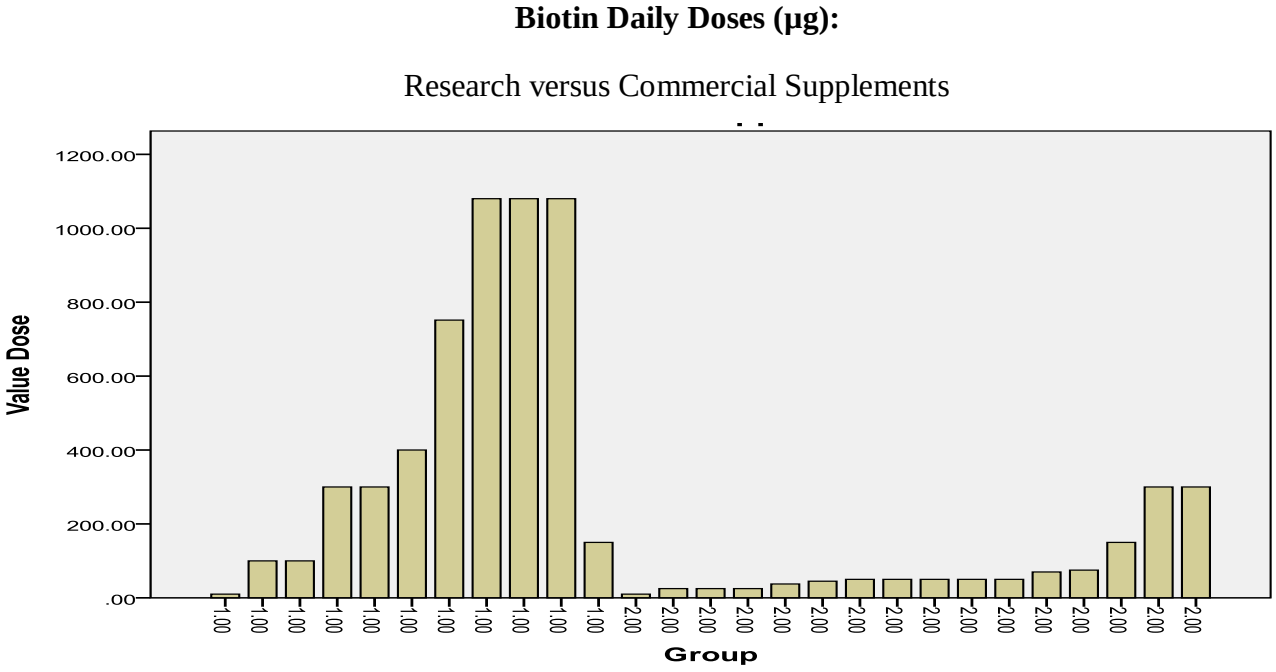


Figure 6. Biotin Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The folic acid median daily dose in research supplements was 560µg and 100µg in commercial supplements. The doses in these two groups were found to be significantly different, *U* (33)= 44.5, *p* = .001*, r* = .57, a difference clearly represented in the dose distribution shown in Figure 7.

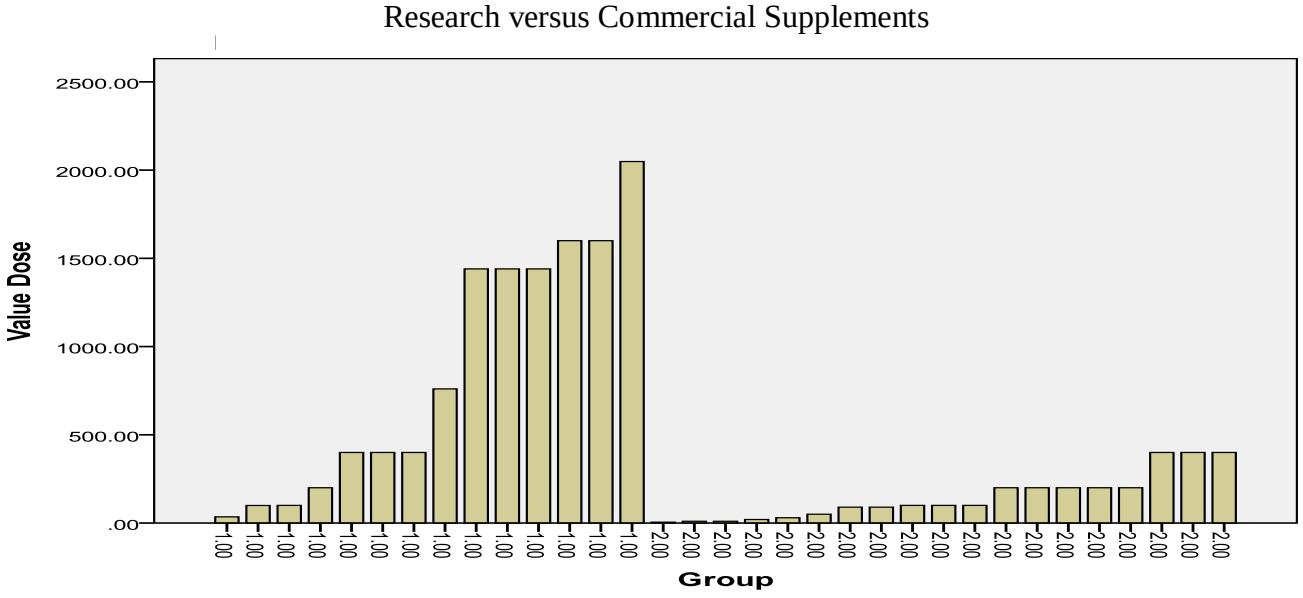


Figure 7. Folic Acid Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The research and commercial daily doses of cyanocobalamin (B_{12}) were found to be significantly different, *U(36)* = 75, *p* < .01, *r* = .45. The median B_{12} dose was 900µg for the research supplements and 5µg in the commercial supplements. This significant difference in daily doses between research and commercial supplements can be seen clearly in Figure 8.

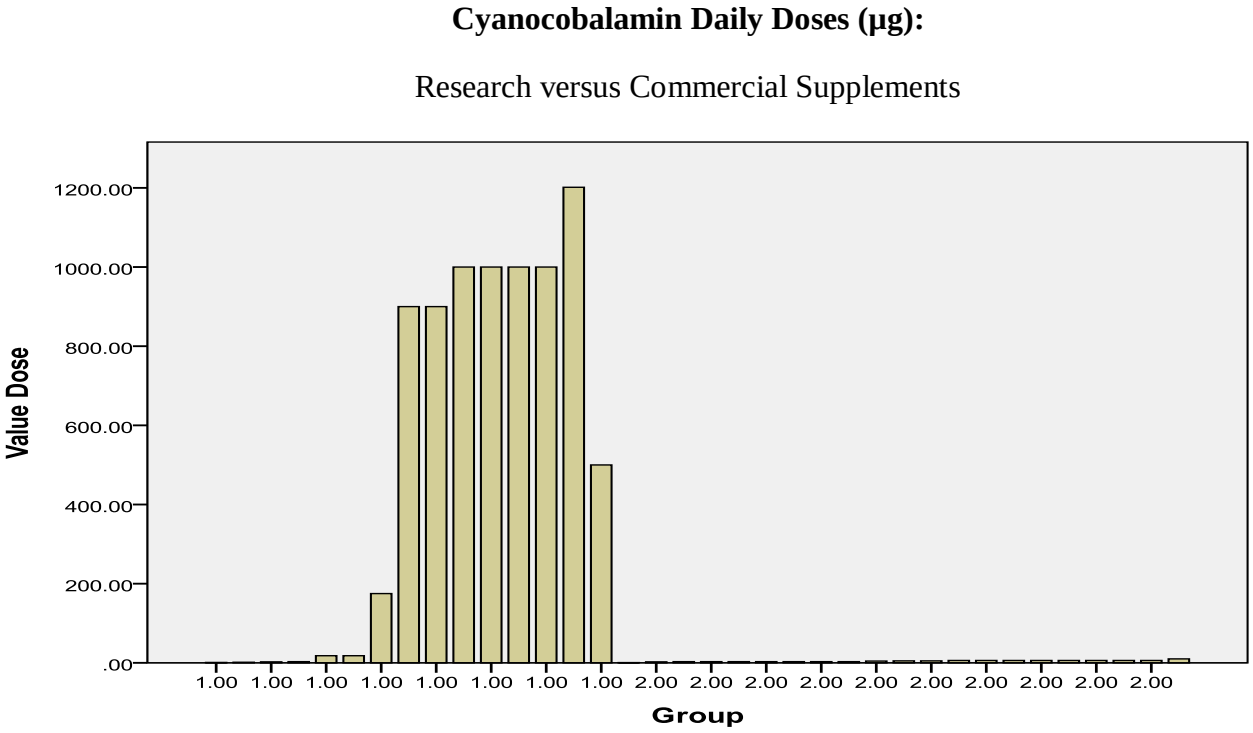


Figure 8. Cyanocobalamin Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

1.2. Vitamins A, C and D

Table 12 displays the daily dose median and range for vitamins A, C and D. The results again indicate that research supplement vitamin doses are higher than doses in commercial supplements. Similarly to the B vitamins, the dose range properties for vitamins A and C also indicate an overall broader dose range in the research supplements when compared to commercial supplements.

The median dose of vitamin A in the research supplements was found to be 1500µg, and in the commercial supplements 900µg. This difference in the research and commercial supplement vitamin A doses was not significant, *U(35)* = 120, *p* = n.s, *r* = .18. The dose distribution of vitamin A in research versus commercial supplements is demonstrated in Figure 9 which indicates more overlap between research and commercial doses than the B vitamins.

Table 12
Vitamin A, C and D Median Daily Dose and Dose Distribution Properties in Research and Commercial Micronutrient Supplements

Vitamin	Research Supplement Median (SD)	Commercial Supplement Median (SD)	Research Minimum-Maximum Dose	Commercial Minimum-Maximum Dose
Vitamin A	1500µg (1416.36)	900µg (861.27)	300 – 4512.8	15 - 3000
Vitamin C	600mg (386.8)	60mg (25.73)	26.6 - 1500	20 - 500
Vitamin D	10µg (13.59)	7.5µg (3.5)	2.5 - 40	2.5 - 360

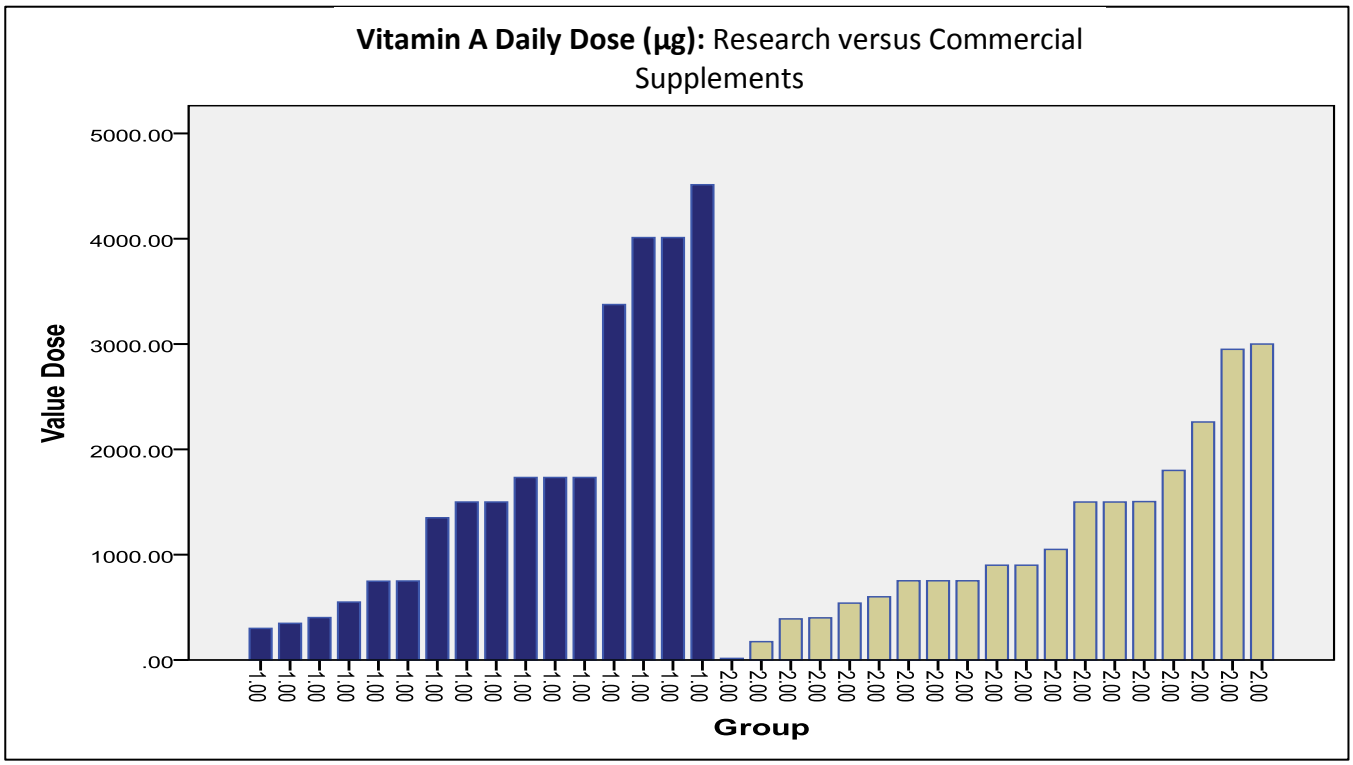


Figure 9. Vitamin A Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The research and commercial supplement daily doses of vitamin C were found to be significantly different, $U(35) = 56.5$, $p < .01$, $r = .52$. The median vitamin C dose was 600mg for the research supplements and 60mg for the commercial supplements. This significant difference in daily doses between research and commercial supplements can be seen clearly in Figure 10.

Vitamin C Daily Doses (mg):

Research versus Commercial Supplements

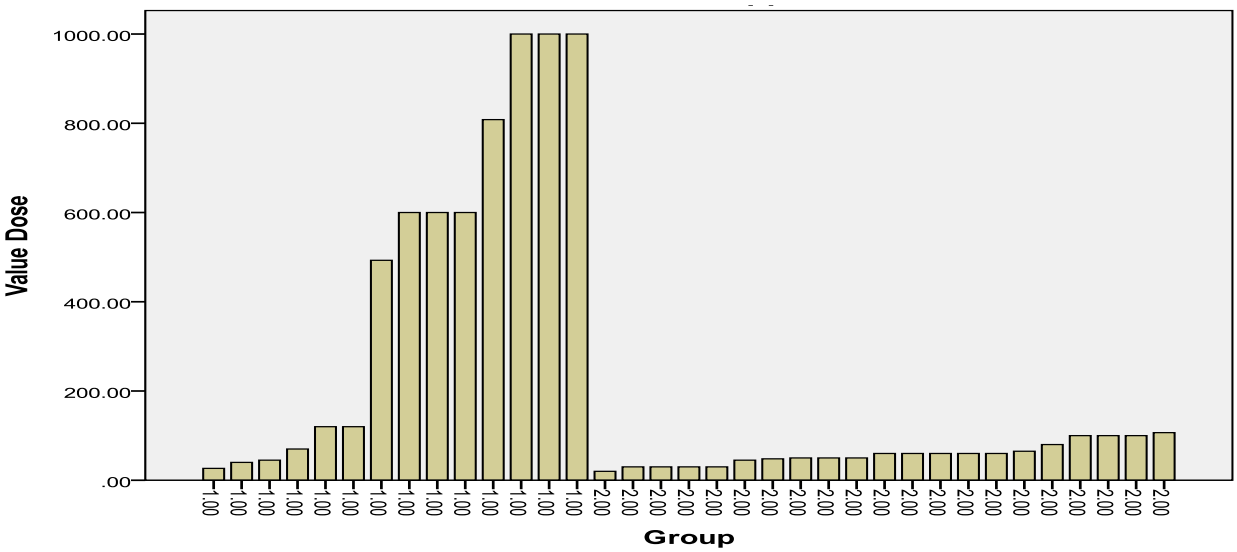


Figure 10. Vitamin C Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

The vitamin D doses in the research and commercial supplements were found to be significantly different, U (33)= 74.5, $p < .05$, $r = .38$. The median daily dose of vitamin D in research supplements was 10µg, and 7.5µg in commercial supplements. This difference is better illustrated in the dose distribution shown in Figure 11.

Vitamin D Daily Doses (µg):

Research versus Commercial Supplements

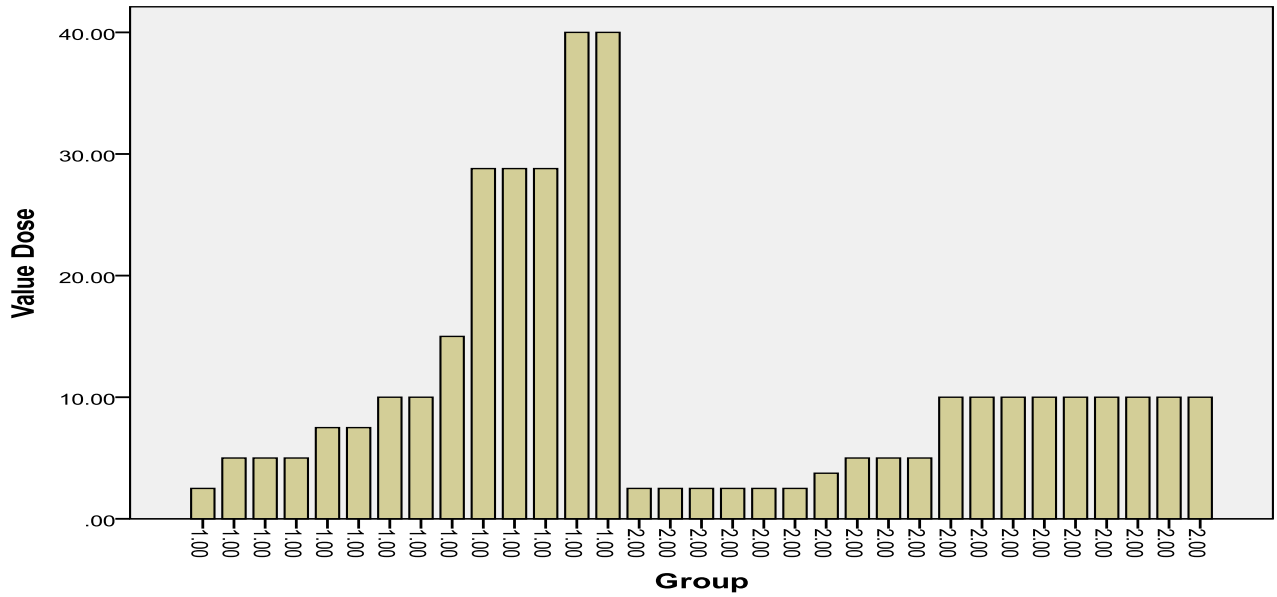


Figure 11. Vitamin D Daily Dose Distribution (Research supplement doses on the left side coded on horizontal axis as 1.00; commercial supplement doses on the right side coded on the horizontal axis as 2.00).

1.3. Outliers

Before using the Mann-Whitney test to assess whether the independent groups (research supplements and commercial supplements) were significantly different from one another, outliers were removed from the data. The initial identification of these extreme data points was done by means of graphical inspection, demonstrated in Figure 12 , where research doses are shown on the left, and commercial on the right. Each colour represents the dose distribution for vitamins thiamin (B_1), riboflavin (B_2), pantothenic acid (B_5) and pyridoxine (B_6). These four vitamins are represented because they are all in milligrams and fall within a similar numerical range. The data points that were removed as outliers, marked with an arrow, are clearly identifiable as extreme in each data set.

The extreme data points that were removed before group comparison analysis are given in Tables 12 and13. A total of 11 vitamins were analysed. From the research supplements six outliers were removed, and from the commercial supplements five outliers were removed. In Table 13 the large difference between these extreme data points and the median dose is clear. For example, the median thiamin (B_1) dose in research supplements was 14.59mg, and the extreme dose declared an outlier was 243.18mg. The next closest thiamine dose in the research supplements was 40.14mg. The biotin (B_7) commercial supplement median dose was 50µg, and the extreme dose

identified as an outlier was 1000µg. The next closest biotin dose was 300µg. The cyanocobalamin (B_{12}) commercial supplements daily dose median was 5µg, and the extreme data point removed before analysis was 750µg. The closest cyanocobalamin dose in the commercial supplements to this extreme value was 10µg.

Table 13
Research Supplement Outliers Removed from Data Analysis

Vitamin	**Median**	**Outlier removed**
Thiamin (B_1)	14.59 mg	243.18 mg
Riboflavin (B_2)	13.5 mg	200 mg
Niacin (B_3)	63.75 mg	750 mg
Pantothenic Acid (B_5)	22.08 mg	450.8 mg
Pyridoxine (B_6)	23.04 mg	287.95 mg
Vitamin C	600 mg	1500 mg

Table 14
Commercial Supplement Outliers Removed before Data Analysis

Vitamin	**Median**	**Outlier removed**
Thiamin (B_1)	1.22 mg	40.84 mg
Biotin (B_7)	50 µg	1000 µg
Cyanocobalamin (B_{12})	5 µg	750 µg
Vitamin C	60 mg	500 mg
Vitamin D	7.5 µg	360 µg

In many cases the Mann-Whitney test results still indicated a significant group dose difference, before the outliers were removed. For example, the research and commercial supplement dose for thiamin (B_1) was found to be significantly different, $U(29) = 36.5$, $p < .01$, $r = .55$. If this data analysis is conducted with the inclusion of the outliers, that is 243.18mg in the research supplement category and 40.84mg in the commercial supplements, the difference would still be significant, $U(31) = 49.5$, $p < .01$, $r = .50$.

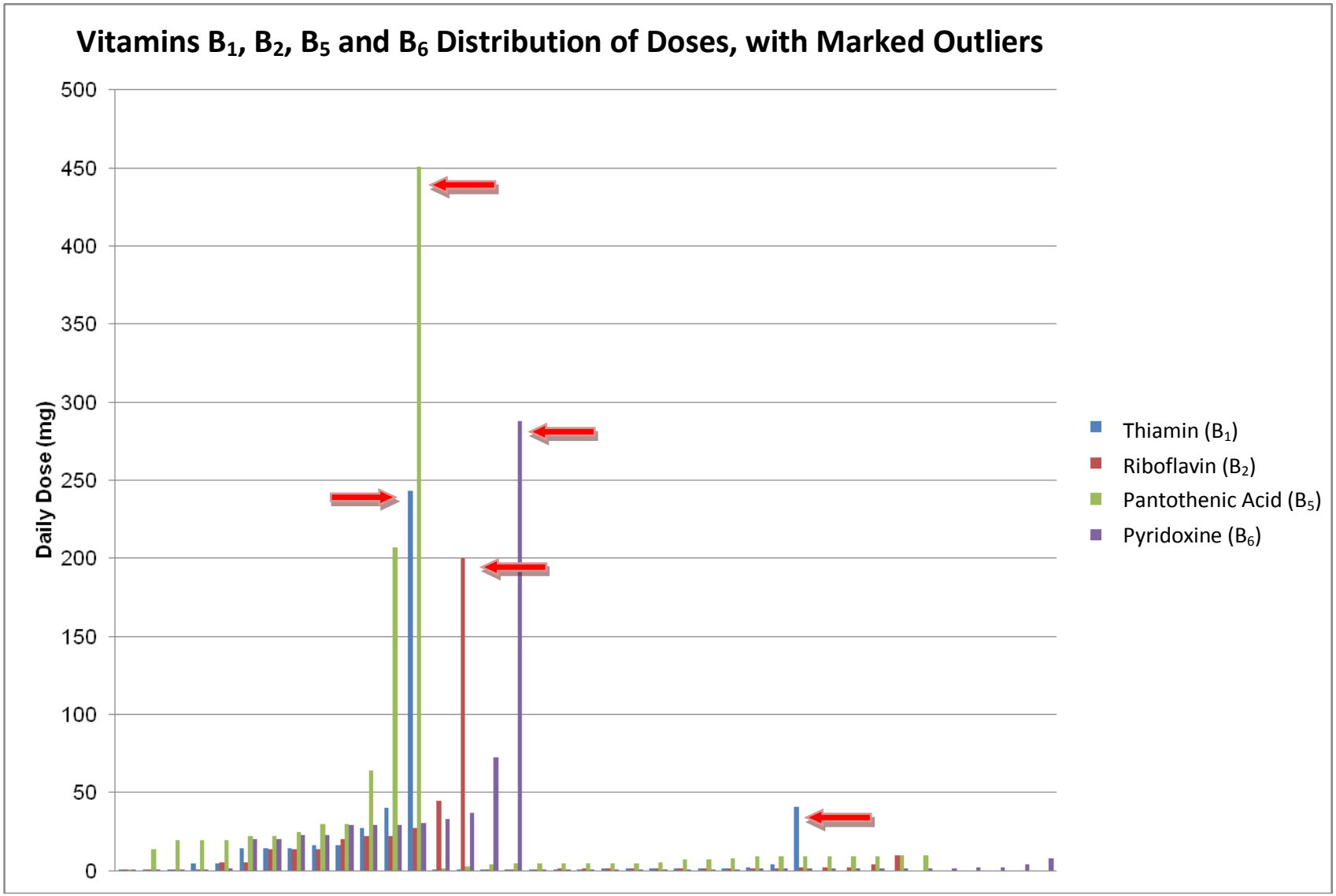


Figure 12: The distribution of doses in vitamins B_1, B_2, B_5 and B_6. The research supplement doses are on the left hand side of the graph, and the commercial doses are on the right hand side of the graph. The arrows indicate the outliers that were removed before the data analysis was conducted.

2. Study 2: Survey

In the following section, an overview of participant characteristics is provided. Then the purchasing habit characteristics of the parents who purchase micronutrients for their child are described, and the rationale surrounding their choice to purchase these nutrients is presented. Thirdly, the parents perceived benefits of micronutrient administration are described.

2.1. Overview of Sample Characteristics

This survey was predominantly answered by females, as female respondents represented 95% of the total participants. A large majority of respondents were married (70%), with the next most common relationship status being in a de-facto relationship (19%). Participants most commonly identified with being New Zealand European (88%), with other European and Maori being the next biggest ethnicity groups. In this sample the distribution of highest qualifications earned was broad, with 29% having earned a bachelor's degree, 23% completed the final year of high school, 14% earned a post graduate diploma, and 13% completed less than final year of high school. 55% of participants had an average gross household income between $35,000 and $99,000, and 31% of participants had an average household income of $100,000 or greater.

Respondents had an average number of 2 children in their care at the time of the study (47%), with one child and three child households equally occurring (21% each). The children's age distribution was as follows: 0-2 years 34%, 3-4 years 36%, 5-6 38%, 7-8 years 29%, 9-10 years 21%, 11-12 years 16%, 13-15 years 20% and 16-18 years 12%. From these children the most commonly reported physical ailments were: 88 who were reported as suffering from asthma, 26 from bedwetting, 71 as suffering from allergies, and eight with eczema. The most common mental health related disorders reported were: 13 with Asperger's, 12 with autism, 11 with dyslexia, 10 children were identified as having an anxiety disorder, nine with ADHD, and eight with auditory processing disorder.

2.2. Who Purchases Micronutrient Supplements?

Out of 365 parents, 232 give their child a multivitamin supplement (64%). A large portion of these parents also gave their child another supplement in addition to a multivitamin. The most common additional supplements parents purchased for their child were vitamin C (100 parents), and fish oil/omega 3 (69 parents). Fifty (22%) of the 232 parents indicated that they did not give their child any supplements in addition to a multivitamin.

Parents reported that their child had taken a multivitamin supplement for a range of time periods: for years 35%, a year 16%, months 27% and weeks 14%. Respondents indicated that 76% of their children take the recommended dosage of their multivitamin supplement. Also indicated was that 18% of children generally were given less than the recommended dosage. The most common child micronutrient brands purchased were Thompsons 40%, Healtheries 28%, Centrum 15% and Blackmores 12%.

In this sample of New Zealand parents, the ethnicity of the participants who indicated they purchase a micronutrient supplement for their child were NZ European 87%, Other European 6%, Maori 4%, Samoan 0.4%, Indian 0.4%, Canadian 0.8%, Australian 0.8% and Other 0.8%. The ethnicity of the participants who did not give their child a multi micronutrient supplement was 82% NZ European, Other European 8%, Maori 6%, Samoan 0.7%, Chinese 1%, Aborigine 0.7%, and Other 1%. An ethnicity comparison between these two groups shows only a minor increase in the representation of Maori and Pacific Islanders in the participants who do not give their child a micronutrient supplement.

Participants were asked to indicate an estimate of the gross household income this question however, was not compulsory. Consequently this question was only answered by 261 participants. Of the 221 participants who give their child a micronutrient supplement and responded to this question, the household income was as follows; 4% earned $16,000 through to $24,999, 5% earned $25,000 through to $34,999, 10% earned $35,000 through to $49,999, 26% earned $50,000 through to $74,999, 17% earned $75,000 through to $99,999, 31% earned $100,000 or greater, and 7% did not know their household income. These results indicate that 74% of participants who gave their child a micronutrient supplement had a gross household income between $50,000 through to $100,000 and above. The gross household income for the 40 participants who do not give their child a micronutrient supplement, was reported as follows; 10% earned $35,000 through to $49,999, 27.5%

earned $50,000 through to $74,999, 27.5% earned $75,000 through to $99,999, and 35% earned $100,000 or greater. Due to the small number of question completers from the participant group that does not give their child a micronutrient, the household incomes reported cannot be relied upon to accurately represent this group.

2.3. Why Parents Administer Micronutrients

The analysis revealed that there are a number of motivators behind the purchasing of child micronutrient supplements. These can be seen in Table 14 which lists the motivators in order of popularity. The most common reasoning was to prevent colds or illnesses, 129 respondents (23%). The other top motivators were: confidence that their child is getting a balanced diet (15%), their child is a picky eater (13%), to improve their child's mental acuity (8%) and because their child is run down (7%). Of the 7% of parents who purchase multivitamins for other reasons, none specified motivators that were psychologically based. Over two thirds (71%) of these parents do not look for anything specific in the multivitamin ingredients when purchasing a supplement. Of those 29% of parents who look for a specific ingredient, the most commonly targeted ingredients were vitamin C, iron and a variety of or high dosage of B vitamins. The most influential factor for parents when choosing a multivitamin for their child firstly was the price, and secondly was their child's preference in taste. These factors were closely followed in popularity by the ease of consumption for their child, whether the supplement is chewable and the supplement brand.

Table 15
Reasons Parents Purchased Multivitamins for their Children

Motivations	Response Number	Response %
Prevention of colds or illnesses	129	24
It gives me confidence that they are getting a balanced diet	86	16
My child is a picky eater	75	14
To improve my child's mental acuity (i.e. their intelligence, cognition)	44	8
Because my child is run down	41	8
Other	39	7
To improve my child's ability to focus	31	6
The doctor recommended multivitamins	26	5
Because I read that multivitamins were good for children	15	3
Because my child has a mental health disorder e.g. ADHD, autism, dyslexia, depression	15	3
Because I was given a multivitamin as a child	9	2
Because my child suffers from a disease	8	2
To help reduce my child's anxiety	6	1
Because a fellow parent recommended them	5	1
Don't know	1	0

Note:
- ***Highlighted areas are psychologically based motivations.***
- ***Participants were asked to choose all reasons that applied to their situation.***
- ***Participant's motivations for purchasing multivitamins for their children are listed in order of popularity.***
- ***Response percentages are rounded to the nearest whole number.***

Parents were able to select or specify multiple reasons for their purchasing of a multivitamin for their child. Respondents reported a range of benefits that they have perceived as a consequence of giving their child a multivitamin supplement. The most commonly reported benefit was that their child gets ill less often or with less severity (113 respondents, 49%). Another benefit commonly perceived was that their child recovered from illness faster (27%). Other benefits parents perceived in their child were: more energy (17%), improved focus (9%), and improved behaviour (9%). Thirty percent of parents who give their child a multivitamin reported seeing no direct benefits.

2.4. Perceived Benefits of Micronutrient Administration

Of those respondents who indicated one of their motivators for purchasing a

multivitamin was to improve their child's mental acuity, 6.8% reported that as a result of their child taking a multivitamin they noticed an improvement in their child's mental acuity. Twenty seven percent of the parents who indicated their reasoning for purchasing multivitamins included to improve their child's mental health disorder, perceived an improvement following their child's use of multivitamins. From those parents who reported that a reason for purchasing a multivitamin was to improve their child's ability to focus, 42% perceived a benefit in their child's focus. Of the six parents who indicated that they purchase a multivitamin to help reduce their child's anxiety, three (50%) reported that they perceived an improvement in their child's anxiety following multivitamin administration. Overall, of those parents whose motivations for purchasing multivitamins were psychologically based, 24% perceived an improvement in the targeted psychological area. In addition, from this group of parents, 15 perceived an improvement in their child's general behaviour. Healtheries was clearly the most popular choice of supplement brand for the parents whose motivations to purchase a micronutrient supplement for their child included a psychologically focussed purpose, with 20% of parents most commonly choosing this brand. The second most popular supplement brand among this group was Blackmores, at 10%.

Discussion

These studies addressed the composition and use of micronutrients given to children. To address this, three aims were investigated across two studies; Study 1, a study of micronutrient composition and Study 2, an examination into the motivation to use micronutrients. The first study consisted of two aims. The first aim was to compare the ingredients of micronutrient supplements that were effective in research to the ingredients in commercial micronutrients. The second aim was to compare the doses in research micronutrients to the doses in commercial micronutrient supplements. There was one aim in Study 2; identify why New Zealand parents give their child a micronutrient supplement.

The discussion will be sectioned according to each research focus. Firstly, describing and discussing the composition of micronutrient supplements in both research and commercial settings. Followed by a discussion of the reasons parents give their child a micronutrient supplement, and the associated characteristics such as perceived

micronutrient benefits and the factors that are influential on the choice of micronutrient supplement brand.

1. Micronutrient Supplement Composition

The composition of ingredients in the research and commercial supplements did not differ greatly. The vitamins appeared in general as frequently in the research products, as they did in commercial supplements. There were some differences in supplement ingredients among the minerals, whereby research supplements were found to include a marginally wider variety of minerals than the commercial supplements. An example of this was molybdenum, which was found in 69% of research supplements, but just 9% of commercial supplements. Prevalence differences similar to those found with molybdenum were also found between the research and commercial supplements for selenium and chromium. Vanadium and boron were not included in the ingredients of commercial supplements; however, they were included in the ingredients of 23% of the micronutrient supplements used in research. The findings indicated that the research and commercial supplements were not greatly different in their choice of vitamin or mineral ingredients with the exception of some minerals.

The minerals found notably more in the research supplements were selenium, vanadium, boron and molybdenum. Selenium plays an important role in thyroid metabolism, therefore it may play a role in psychological facets, for example irritability and tiredness (Arthur, 1991). Vanadium, boron and molybdenum however, are not commonly discussed as playing major roles in mental and psychological health (Young, 2002). The before mentioned mineral roles in psychological health indicate that the differences in effectiveness that may be suggested between research and commercial supplements, are not likely to be contributable to the choice of minerals or vitamins in supplements, as the vitamins and minerals have in general, a similar occurrence across the research and commercial supplements. It should be noted that this comparison did not take into account the different forms of each vitamin or mineral used in the supplements. If the comparison had been adjusted to also reflect the different forms of the nutrients, the ingredient frequency findings may have been different between the research and commercial

supplements, however due to the time constraints of a Master's thesis has not been further investigated.

The vitamin included in all the supplements analysed was pyridoxine (B_6), indicating that pyridoxine may play an important role in the combination of nutrients used in micronutrient supplements. Pyridoxine is involved in the synthesis of a number of neurotransmitters including serotonin, dopamine, acetylcholine, norepinephrine and GABA (Dakshinamurti et al. 1990). These neurotransmitters are heavily associated with depression, mood, sleep, attention, appetite, and anxiety (Tasman et al. 1997). Although, pyridoxine was included in all of the analysed supplements, the median dose of pyridoxine was significantly different between the research and commercial supplements. The median commercial daily dose approximated the RDI dose of 1mg for New Zealand children aged between 9 and 13 (NHMRC, 2006), the median daily dose in research supplements was much higher, at approximately 23mg. The higher research supplement dose may indicate that B_6 levels significantly above the RDI are necessary to effectively impact on mental and emotional psychological symptoms.

Following vitamin B_6 in popularity in supplement ingredients was vitamin B_{12}. B_{12} was included in the ingredients of all commercial supplements sampled, and almost all of the research supplements indicating that B_{12} may also play an important role in the combination of ingredients used in micronutrient supplements. The psychological effects of B_{12} deficiency include adverse effects on cognition from adolescence years onwards (Louwman et al 2000), indicating that B_{12} may have a role in the improved cognition found in the multiple cognition studies discussed. The RDI for New Zealand children aged between 9 and 13 is 1.8µg (NHMRC, 2006), which is lower than the 5µg commercial supplement daily dose median and significantly lower than the research median dose of 900µg. The notable difference indicates that achieving a significant change in mental and emotional symptoms may require B_{12} doses significantly greater than the RDI for New Zealand children.

The median daily doses were found to be greater in the research supplements than the commercial supplements across all of the vitamins analysed, these included the vitamins: A, B_1, B_2, B_3, B_5, B_6, B_7 (biotin), B_9 (folic acid), B_{12}, C, and D. These differences were revealed to be significant by a non-parametric, two-tailed Mann-Whitney test for all of the vitamins with

the exception of vitamin A and riboflavin (B_2). The median vitamin A daily dose was found to be 1.7 times greater than the commercial daily dose. This difference was not significant, with a p value of approximately 0.3. Although more overlap is shown in the graphical representation of the daily doses with a significant group difference(see Figures 1,3,4,5,6,7,8,9,10, 11), a greater overall dosage is still noticeable in the vitamin A research doses (see Figure 9), a finding which is also true for B_2 (see Figure 8). These results indicate that research and commercial micronutrient supplements have significantly different vitamin dosage compositions. The most important ramification of this significant difference may be the inability to generalise micronutrient research findings to over-the-counter commercially available micronutrient supplements.

For New Zealand parents, this means that the micronutrient supplements available in supermarkets, health food stores and pharmacies, are unlikely to be as effective as the supplements used in research when targeting behavioural change. A number of micronutrient products available in New Zealand indicate that their ingredients have psychological benefits. Although the characteristic information of the nutrient that they present is correct, the information may also be misleading. Based on research supplement composition, it appears that the psychological benefits found as a result of micronutrient administration are obtained through doses much higher than the doses in the micronutrient supplements that they have provided the information in conjunction with. For example, the company Kordel, includes this quote in their on-line product information for Kordel's Smart Multi: "Nutritional research indicates that infants and children with increased DHA intakes have higher IQ scores, improved cognitive function, learning abilities and behavioural skills." The DHA dose in this Kordel multivitamin supplement is 26mg. In the 2008 study investigating whether DHA supplementation was linked to improved cognitive skills, the effective daily dose amount of DHA given to preschool participants was 400mg (Nelson, 2008). Although the product does not claim to provide these results, the inclusion of this information with the product's description may lead consumers to think that this product would produce a similar effect, which is unlikely when the product dose is significantly lower when compared to the effective research dose.

The most significant differences in doses between research and commercial supplements were found to be in pantothenic acid (B_5) and folic acid (B_9). The significantly

larger research supplement doses of pantothenic acid and folic acid are unsurprising given their roles in mental health.

Pantothenic acid has a number of important roles in mental and psychological health. As a component of CoA, pantothenic acid plays an important role in the synthesis of vitamins A and D and neurotransmitters, and when combined with choline produces acetylcholine, a neurotransmitter with important roles in memory, attention and cognitive functions (NHMRC, 2006). The median dose amount in research supplements was found to be approximately four times higher than the AI of 5mg for boys and 4mg for girls. The dose in commercial supplements was much closer to the AI, with a median daily dose of 7.5mg.The high dose found in research supplements is unlikely to cause adverse health effects as there have been no indications of adverse health effects in either humans or animals (Wellington: Ministry of Health, 2011).

Folic acid also plays a key role in psychological processes. It is used in the manufacturing of neurotransmitters, and is a cofactor in the synthesis of serotonin. Folic acid is vital in helping to maintain normal serotonin levels; consequently, depression is a common symptom of folic acid deficiency (Alpert, 1997). The median research daily dosage of 560 µg is 260µg above the RDI (NHMRC, 2006) for children aged between 9 and 13. Although much higher than the 100µg commercial supplement median, the research daily dosage is still well below the LOAEL, which was set at 5mg daily (NHMRC, 2006).

The Journal of the American Medical Association (JAMA) (Fletcher & Fairfield, 2002) showed that the North American Diet, while sufficient to prevent vitamin deficiency diseases, is inadequate to support optimal health. Fletcher and Fairfield also noted a growing concern among nutrition experts that the RDA's for vitamins and minerals are too low. The United States RDA guideline levels in 2002 were similar overall to those set by the NHMRC (2006) guidelines, with the RDA of some vitamins in the New Zealand guidelines set marginally higher, and others marginally lower. The American RDA levels are established to prevent acute vitamin deficiency disorders however evidence suggests that higher levels of many vitamins and mineral are necessary to achieve optimum health (MacWilliam, 2009).

The assessment made by the JAMA that RDA values are set too low, is supported by the almost unanimously higher median vitamin daily dose's (with the exception of niacin and

folic acid in the commercial supplements) found in both the research and commercial supplements. This difference was most evident in the median research cyanocobalamin dose which was found to be 500 times greater than the RDA set by the NHMRC (2006) guidelines. This high vitamin intake is unlikely to produce adverse effects, possibly because of the body's ability to decrease absorption in response to high intakes (UK Expert Group on Vitamins and Minerals, 2002). The commercial median daily dose was also greater than the RDA, at 2.8 times greater than the recommended daily dose.

It is possible that the dosages in commercial supplements are significantly lower than the dosages in research supplements due to the increased cost of larger nutrient doses, and the cost of superior raw materials used in the preparation of the research micronutrient products. There were 13 effective research supplements and the prices were available for two of these. Using these supplements as a cost guide for the research supplements, the average cost of a research supplement when used in a treatment setting was $6.90 daily. The average price of the 22 commercial products was 64cents for a daily dose. This large difference in the daily cost of providing a child with a micronutrient supplement is likely to be a significant reason for the low doses found in commercial products, as it is unlikely parents are willing to pay for higher doses. This is supported by the survey finding that price may be the most influential factor when New Zealand parents are choosing a multivitamin for their child.

2. Motivations Behind Micronutrient Use

Eighteen percent of parents identified a psychologically based reason as one of their key motivations for purchasing a micronutrient supplement for their child. This low percentage of parents confirms the hypothesis that the majority of parents in New Zealand do not purchase a micronutrient supplement to improve their child's psychological well-being. Parental motivations for purchasing micronutrient supplements were found to be largely based on physical health. The most common motivating factors for a New Zealand parent to purchase a micronutrient supplement were the prevention of colds or illnesses and the confidence it gave them that their child was getting a balanced diet.

The survey results suggest that efficacy at the commercial supplement doses is not present, as overall just 24% of parents whose motivations for purchasing multivitamins were

psychologically based, perceived an improvement in the psychological area they were targeting. This indicates that the parents who give their child a supplement for a psychologically based reason do not perceive a behavioural modification after supplementation. It is possible that this finding is not completely accurate as parental perceptions without a methodologically sound measuring tool may not accurately perceive changes in their child's behaviour. Changes resulting from micronutrient supplementation in physical symptoms such as how often a child gets a cold or flu, are easier for parents to perceive as they can compare of how often the child has a cold or flu compared to the child's friends. It is possible that this ease of reference of change is reflected in the 49% of parents who identified that their child gets ill less often or with less severity following micronutrient supplementation.

The survey identified that a number of parents (18%) generally give their child less than the recommended dose of a micronutrient supplement. The lower dosages some children receive may provide an additional reason as to why parents in general do not perceive psychological benefits from their child's micronutrient use. For parents this may be a price sensitive choice, as parents indicated the most influential factor when selecting a multivitamin was the price.

3. Strengths and Limitations

3.1. Strengths of Study 1.

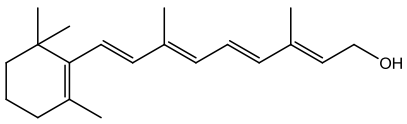
A strength of this analysis was the wide range of New Zealand over the counter supplements that were sampled. The sample of products contained 12 different brands of micronutrient supplements sold over the counter in New Zealand. This broad sample of supplements might mean that the commercial supplement characteristics calculated in this study are highly representative of the micronutrient products aimed at children that are available over the counter in New Zealand.

3.2. Limitations of Study 1.

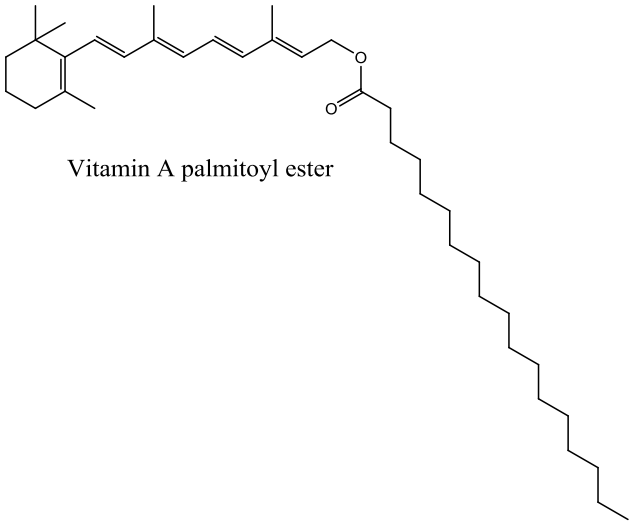
There are a number of limitations involved in this micronutrient supplement analysis. The first of these is that the frequency of nutrient inclusion comparison, did not account for the different forms of each nutrient. The vitamins and minerals were found in a number of different forms across the supplements. In-depth analysis of the forms of each

mineral and vitamin may provide further important information to guide a decision as to whether or not these ingredients are comparable. This in-depth analysis is important because the form of a nutrient indicates the amount of specific mineral or vitamin contained. For example, retinyl palmitate which is a form of vitamin A, contains 54.7% of vitamin A compared to; retinol acetate, which contains 87% of vitamin A (NHMRC, 2006).

A further limitation of this study was using the pure vitamin component for the dose calculations. This is not representative of the amount of vitamin that would be readily absorbed after entering the body, as different forms of a nutrient can have differing levels of absorption. The bioavailability is affected by the polarity (water solubility) of the compound. For example, the palmitoyl ester of vitamin A shown in Figure 13, is very much less polar than vitamin A itself, which will significantly affect it's absorption from the gastrointestinal tract and thus it's bioavailability. When there are significant differences in the bioavailability of forms of a nutrient, it would make a noticeable difference to the pure vitamin dose amount if it was to be altered to reflect the nutrient absorption properties. To remedy this problem, further data analysis would be required. Each type of vitamin would need to be adjusted according to its bioavailability, before conversion to the active vitamin compound dose.



Vitamin A



Vitamin A palmitoyl ester

Figure 13: The molecular structure of vitamin A and vitamin A palmitoyl ester. A demonstration of the difference in their bioavailability.

The largest limitation of this study is a result of to the large number of ingredients contained in the supplements. There were 73 other ingredients and 17 minerals recorded across the range of supplements. Within some of the minerals or other ingredients are ingredients that contain vitamin components that have not been included in the total vitamin doses. The reason the vitamin components were not extracted from these ingredients was the complexity involved in identifying the correct chemical formula used in each ingredient variation within the other ingredients and minerals, and the inability to complete this task within the time constraints of a Master's thesis. To obtain the most accurate median vitamin dose in both the research and commercial supplements, the active compounds need to be calculated for every ingredient in every supplement.

The lack of randomised double blind, placebo controlled trails in the scientific literature, especially in the treatment of psychological disorders, also places a limitation on this study. All study types were included when identifying effective research supplements for analysis in this study. The most common types of studies included in the analysis were open label. An open label study describes the situation when both the researcher and the participant in a research study are aware of the type of treatment the participant is receiving. The largest problem with these trials is the possible expectancy effect that can occur as a result of the symptom evaluator knowing that the child is receiving a supplement. In some of the studies included in the analysis the parents were the sole evaluator of behaviour during the trial period (Kaplan et al. 2002).

The commercial supplements sampled were randomly selected from those available over the counter in New Zealand, and a small sample of popular micronutrient supplements available over the counter in the US, UK and Australia. The analysis did not include all micronutrient supplements available in New Zealand. An attempt was made to include a child directed micronutrient supplement from all brands sold over the counter in New Zealand, to attempt to ensure that the sample used in this analysis was be an accurate representation of what is available over the counter in New Zealand.

Notwithstanding these limitations, the results of this study clearly suggest that differences in composition between effective research micronutrient supplements and commercial supplements do exist.

3.3. Strengths of Study 2.

A strength of this survey was the large sample size. The minimum number of survey respondents this survey aimed to recruit was 100 participants who purchase micronutrients. This survey had 365 participants, 232 of which purchased a micronutrient supplement for their child, surpassing the minimum number of participants sought.

A web based survey was the most practical approach to this data collection, as the literature suggests it is the most efficient method for the least biased participant responses and the best option for optimising subject recruitment, especially in terms of sample size (Krantz & Dalal, 2000). Research suggests that there is little difference in the data collected by web based surveys when compared to traditional methods (Krantz & Dalal, 2000). An advantage of using a web based survey was that participants could access and complete the survey in their own time, 24 hours a day. An additional benefit was that the recruitment process is simple, with advertising in the form of an on-line link which makes the survey readily accessible, and as reflected in the participant numbers, these advantages naturally produce higher survey participation.

3.4. Limitations of Study 2

This survey was predominantly answered by females (95%), meaning 5% of respondents were male. Although this represents a skewed sample of the population, it may not affect the results of the survey as the key points of interest were parents purchasing habits of micronutrients for their children, with a focus on parent's key motivations for purchasing micronutrient supplements for their child.

In this sample of New Zealand parents, participants were not accurately representative of the New Zealand population. The distribution of ethnicities in New Zealand in 2006 were NZ European 67.6%, Maori 14.6%, Australian 0.7%, Other European 2.5%, Asian 8.8%, Pacific Island 6.6% and Other 0.9% (Statistics New Zealand, 2006). The distribution of ethnicities in this sample were New Zealand European (88%), with the next biggest ethnicity groups being Other European followed by Maori. These participant characteristics indicate an over-representation of NZ Europeans in this sample. This reduced diversity in survey respondents will limit the usefulness of the survey findings when used in some settings. An example of a setting where the survey results may have restricted use is if the results are being applied to

identify ethnicity groups that are low micronutrient users, possibly to target specific groups for the purpose of introducing micronutrient supplementation as a treatment option.

Another limitation of this study is sample selection bias. The sample of parents in this study may have been a selected sample from a group of higher income earners as participants had to have access to a computer. The sample may also contain more parents interested in the effects of micronutrients. Both of these groups may be more likely to purchase a micronutrient supplement for their child. If this has occurred, the demographic characteristics may be skewed and the percentage of New Zealand parents who give their child a micronutrient supplement may also be higher than in a balanced New Zealand cross section. The demographics of parents and percentage of micronutrient users, was not however the main aim of the survey investigation and these imbalances should not have affected the reported motivations of parents who purchase micronutrient supplements.

4. Implications and Future Directions

4.1. Implications

There is a large difference in the daily cost of providing a child with a research standard micronutrient supplement compared to a standard commercial supplement, and it is unlikely parents are willing to pay for the higher doses. This theory is supported by the survey finding that for New Zealand parents price was the most influential factor when choosing a multivitamin supplement for their child. This is a concern. Research has shown that nutrients including saturated fats, trans-fats and added sugars that are associated with higher disease risk are also associated with lower diet cost (Aggarwal, Monsivais, & Drewnowski, 2012). Conversely, they also showed that nutrients such as dietary fibre, vitamins A, C, D, E and B12, folate, iron, potassium and magnesium, are associated with higher diet costs, and a lower risk of chronic disease. These findings indicate that lower intakes of beneficial nutrients are associated with lower diet costs. Aggarwal, Monsivais and Drewnowski (2012) found that persons with lower cost/lower quality diets were more likely to be from lower socioeconomic (SES) groups, a concerning association as it suggests that the SES groups most in need of micronutrient supplementation in their diet, may currently be the least likely to purchase a micronutrient supplement.

In order for micronutrient supplements to be a viable dietary option for New Zealand parents trying to help their child improve their cognition or psychological symptoms, the overall cost of effective micronutrient supplements would need to be significantly reduced as sustaining the cost of these effective nutrients over a prolonged period of time may be difficult for many families. The approximate cost of an effective supplement for use in targeting physical health or mental health issues would be $207 monthly, an amount that may be unlikely to be paid by New Zealand parents for whom the most influential factor on their supplement purchasing may be price. The consumer market is currently paying on average for an over the counter supplement, $19.20 monthly. The monthly cost of giving a research grade supplement to a healthy child without targeting physical or mental health symptoms using eight EMPowerlpus capsules taken daily as a reference, would be approximately $102, which continues to be much greater than current over the counter supplement costs. Government or insurance subsidisation would be one way to decrease supplement costs for families. Before support in the form of a subsidy could be explored, extensive randomised controlled, double blind testing of micronutrient supplements would be necessary, in order for micronutrient supplements to be recognised as a viable treatment option with proven efficacy.

It is important that the public are aware of micronutrient supplements as a possible treatment option or supplementary treatment option for mental or emotional symptoms. Micronutrients provide a natural treatment option for children, that in some cases can enhance pharmacological drug effects (Simpson et al, 2011), or can act on their own to significantly improve psychological symptoms. Another benefit of micronutrient supplements is if a child has any other concerning health disorders or diseases for which they are already receiving treatment, a micronutrient supplement used to treat psychological symptoms may be less likely than the alternative pharmaceutical intervention to interact with pharmaceutical medications already taken by the child. Although parents were able to provide multiple reasons for which they purchase a micronutrient supplement for their child, the survey revealed that the majority of New Zealand parents are likely not aware of the psychological benefits that micronutrients can provide. If future research findings continue to support the efficacy of micronutrients when used in a psychological

treatment setting, then a concerted effort should be made by practitioners to provide micronutrients as a treatment option to their patients.

4.2. Future Directions

Future research may initially focus on determining how micronutrient supplements can cause behavioural change. The mechanism by which these supplements are achieving the significant results found in most of the research to date, may be contributable to what is called a 'pharmacological cocktail' effect (ie. when a mixture of chemicals is required for an effect). Micronutrient supplements vary in both ingredients and dosages which makes it difficult to identify the best micronutrient supplement composition, but an advantage of these varied supplements is that they do provide a point of comparison to help identify which nutrients may be essential. To identify the most effective nutrient combinations extensive testing is required of different nutrient combinations at different dosages, achieved through eliminations and additions of ingredients; and dose reductions and increases until a formula which optimises results is found.

The next stage of micronutrient research may focus on the best approach to micronutrient supplements used in a treatment setting. One approach to micronutrient supplement treatment would be to identify the most effective combination of nutrients and their dosages in relation to the treatment goal. For example, a micronutrient supplement used in the context of mood disorders might have a different composition to the micronutrient supplement used in the treatment of anxiety disorders.

Another possible approach to the use of micronutrients as a treatment for psychological symptoms or improving cognition, is to use the supplement as a nutrient balance correction tool. It is possible that nutritional status influences the response to supplementation as hypothesised by Schoenthaler and Bier (1999) and Schoenthaler et al. (1991; 2000). Therefore in some studies perhaps those that did not respond to supplementation had a better diet. The reason micronutrient formulae demonstrates benefits may be due in part to an underlying dietary inadequacy. This theory is supported by human physiology and nutrition theory, which shows that cellular brain functioning is partially dependant on nutritional status (Essman, 1987). This requires further research as not all studies have supported this theory (Osendarp et al. 2007). Exploration of this

possibility requires further blood tests to identify nutrient imbalances in the individual and following this, the micronutrient supplement would be tailored to the individual to correct these imbalances.

Replications of effective research studies are also required for the advancement of micronutrients used as a psychological treatment. These replications need to assess affects over an extended period of time, and continue to explore the reduction in the amount of supplement administrated over longer periods. Further exploration into the maintenance of treatment effects with reduced supplement intake, is important from a cost perspective for the family, and for the child. In the long term it will mean that a child will not need to swallow as many pills. In one of the research studies, the number of pills administered to a child once their symptoms reduced significantly was reduced to 25% of the full dose, and the significant behavioural changes were found to be maintained two to three years following the end of the study (Kaplan et al., 2002).

Further research with a balanced cross section of New Zealand parents in terms of household income and ethnicity may need to be carried out. This research would be necessary to confirm that the motivational reasons identified are representative of how all groups of New Zealand parents think. It would also provide a more accurate picture of the prevalence of micronutrient use among children in New Zealand, which would be helpful when using this study to guide the targeting of groups if wanting to provide micronutrient supplements as a treatment option. Future research should also assess in more detail the perceived benefits of micronutrients, by asking specific questions. For example, a follow up question if a respondent indicated a perceived cognitive improvement in their child may be: in which of the following cognitive areas have you perceived an improvement; language, memory, perception, categorisation or thinking? This research should also examine why parents do not buy their child a micronutrient supplement, which would provide further insight as to how much New Zealand parents know about the roles of micronutrients, which would help to guide practitioners if they wanted to recommend micronutrients, in their approach to introducing micronutrients as a treatment option.

The attitude towards dietary supplements by journals needs to adjust in support of the furthering of supplement research. This is necessary in order to attract the monetary

support for further micronutrient research and to increase the public awareness of dietary supplements as an effective psychological treatment. The approach by journal publications towards dietary supplements has been found to have a relationship with the amount of pharmaceutical advertising in a journal (Kemper & Hood, 2008). In an analysis of 11 major medical journals, increased pharmaceutical advertising was found to be associated with fewer published articles about dietary supplements, and the publishing of more articles with conclusions that dietary supplements are unsafe (Kemper & Hood, 2008). These obstacles to both funding and publishing this type of work should be removed, as micronutrient supplements continue to demonstrate reduced adverse side effects (Katz et al. 2010; Mehl-Madrona et al. 2010; Simpson et al. 2011) and effective results in psychologically based research.

5. Conclusions

The current study has investigated the composition of micronutrient supplement ingredients, the use of micronutrient supplements by New Zealand children, and through a literature review has shown that micronutrient supplements effectively ameliorate a wide range of behaviours in children. This research has demonstrated that micronutrient supplements found to be effective in research with a child based psychological focus in general have significantly greater vitamin dosages than commercially available supplements. Furthermore, it was found that micronutrient supplements are not generally given to New Zealand children for psychologically based purposes.

As observed in the current study, comparing the ingredients and dosages in micronutrient supplements is a complex process, and although significant differences were identified, the accuracy of these values are not absolute. Therefore future research aiming to establish the exact values of vitamins and minerals contained in supplements is needed. In the calculation process this would require taking into account the absorption of different forms of nutrients and the nutrient components in other ingredients.

Assessing the efficacy of micronutrient formulas will require extensive research. It is likely that eventually different micronutrient supplements will be formulated for which the safety and efficacy are optimised to the metabolic requirements of treating different

disorders, different individuals, different ages, and different co-morbid health situations (Popper, 2001).

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Appendices

Appendix A

Statement of Voluntary Consent

To participate in the study described below.

Name of Study: Examination of Micronutrients for Children: their ingredients, the parents who purchase them, and the role they play in psychological well-being.

Purpose of the Study: To better understand parent's motivations when giving their child a micronutrient supplement, and the factors that influence their purchasing of micronutrient supplements.

Any questions, feel free to contact either of the primary researchers.

Primary Researchers: Amy Harris and Julia Rucklidge.

Contact Information: Department of Psychology

University of Canterbury

Private Bag 4800

Christchurch 8140

arh85@uclive.ac.nz

julia.rucklidge@canterbury.ac.nz

The estimated time of completion for this survey is 5 minutes, although this time can vary depending on the participant.

As a volunteer participant in the above mentioned research, I understand that I will be asked to complete a survey that will ask questions related to my households use of micronutrients and my feelings surrounding this. It will also ask questions of a demographic nature. This is to estimate how representative the sample is, of the NZ

population. I also understand that I may consider some of the questions personal in nature but that the information I provide will be used exclusively for this study and will in no way be associated with my name, computer log-in or any other identifiable information.

This survey is a part of the completion of an MSc thesis, which will be a public document accessible via the UC library database.

Participants who do not have children are not eligible to complete this survey.

By clicking “I Agree”, I state that I have read this consent form in its entirety and that I understand that I am able to exit the survey at any point, without saving, and without consequence.

- I Agree
- I Do Not Agree

This study has been approved by the Human Ethics Committee at the University of Canterbury.

Appendix B

Child Multivitamin and Mineral Use Survey

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

1. **How many children currently reside in your household? Note: A child is defined as any person under the age of 18.**

If there are no children living in your household you will automatically exit the survey at this point.

0

1

2

3

4 or more

2. **Are you a male or female?**

Female

Male

3. **What is your date of birth? (DD/MM/YYYY)**

_____

4. **What is your marital status?**

Married

Divorced

Separated

Single

De Facto

Civil Union

Widow

5. **Which ethnicity/ethnicity's do you most strongly identify yourself with? (Please select all that apply)**

New Zealand European

Other European

Maori

Samoan

Cook Islands

Tongan

Chinese

Indian

Japanese

Korean

Other (Please Specify)

6. **Do you live in New Zealand?**

Yes

No

7. **What is the age or ages of the children living in your household? Choose all categories that apply.**

0-2 yrs

3- 4 yrs

5- 6 yrs

7-8 yrs

9- 10 yrs

11- 12 yrs

13- 15 yrs

16- 18 yrs

8. Do any of the children in your household have any of the following?

Dyslexia

Attention Deficit Hyperactivity Disorder (ADHD)

Attention Deficit Disorder (ADD)

Mood/ Bipolar Disorder

Depressive Disorder

Asthma

Allergies

Autism

Aspergers

Bed wetting

Auditory Processing Disorder

Downs Syndrome

Other (please specify)

9. Do any of the children in your household take multivitamins?

Yes

No

10. Do any of the children in your household take any other type of supplement? Choose all categories that apply. (If answered no to question nine, participants were sent to question eighteen after answering question ten).

Note: A child is defined as any person under the age of 18.

Fish oil/ Omega 3

Vitamin C

Echinachea

Immunity booster

Other (please Specify)

They do not take any supplements

11. For approximately how long have they taken a multivitamin?

Days

Weeks

Months

A year

Years

Don't Know

12. Do they generally take the recommended dosage of their multivitamin? Note: This question is asked as an aspect of this research is investigating whether the recommended dosage is effective.

Yes, they generally take the recommended dosage

No, they generally take more than the recommended dosage

No, they generally take less than the recommended dosage

They generally take more than the recommended dosage only when feeling sick

13. For what reasons do you buy your child(ren) a multivitamin? Choose all categories that apply.

It gives me confidence that they are getting a balanced diet

The doctor recommended multivitamins

Prevention of colds or illnesses

To improve my child's mental acuity (i.e their intelligence, cognition)

Because I was given a multivitamin as a child

My child is a picky eater

Because my child suffers from a disease

Because my child is run down

Because I read that multivitamins were good for children

Because my child has a mental health disorder e.g. ADHD, autism, dyslexia, depression

To improve my child's ability to focus

Because a fellow parent recommended them

To help reduce my child's anxiety

Other (Please Specify)

Don't Know

14. What brand of multivitamin do you most often purchase?

Healtheries

Centrum

Blackmores

Natures Own

Thompsons

Radiance

Solgar

Natures Sunshine

Kordel's

Nature's Plus

Other, (please specify) _____

Not sure

15. Is there something specific in the ingredients that you look for, when choosing a multivitamin supplement?

No

Yes. Please specify the ingredient(s) _____

16. What factors are most influential in your choice of multivitamin? Choose all categories that apply.

Price

Brand

Convenience or ease of consumption for my child

Word of mouth

Child's preference in taste

Child's preference in packaging

Other (please specify)

Not sure

17. Have you perceived any benefits from your child(ren) taking a multivitamin? Choose the categories that apply.

My child has more energy

They get ill less often, or with less severity

Their ability to focus has improved

Their mental health (for example ADHD) symptoms are reduced

My child's recovery from illness is faster

They have less anxiety

They have improved mental capabilities

No, I haven't

Other (please specify)

18. What is the highest qualification you have earned?

Final year of high school

Apprenticeship certification

Less than final year of high school

Post Graduate Diploma

Bachelor's Degree

Master's Degree

Doctorate

Other (Please specify)

19. In what kind of industry do/did you work? (For example: hospital, at home parent, newspaper publishing, child care, mail room, factory work, reception, engine manufacturing.)

_____

20. Roughly what is the household income, before taxes and other deductions, over the last 12 months?

Less than $5,000

$5,000 through $11,999

$12,000 through $15,999

$16,000 through $24,999

$25,000 through $34,999

$35,000 through $49,999

$50,000 through $74,999

$75,000 through $99,999

$100,000 and greater

Don't Know

Appendix C:

An excerpt from my full ingredient micronutrient table.

				Kumar M. & Rajapopalan S. 2008		Sandstead, H. et al., 1998		Dvorchik, S. et al., 2007		Harrell R. et al., 1981		Xia, R. 2011		Nelson M. et al., 1990		Schoenthaler et al., 2000		Harding et al., 2003		Sinn & Bryan, 2007	
Volume Taken Daily				Dose	Daily Dose	Dose	Daily Dose	Dose	Daily Dose	Dose	Daily Dose	Dose	Dialy Dose	Dose	Daily Dose	Dose	Daily Dose	Dose	Daily Dose	Dose	Daily Dose
2> 8 years old				1	1	1	1	1	1	6	6			1	1	1	1	1	1		
>8 years old				1	1	1	1	1	1	6	6	1	3	1	1	1	1	1	1	1	1
Ingredients																					
Vitamins	From																				
Vitamin A				1342 IU	1342 IU											750 µg	750 µg			175 IU	175 IU
	Retinyl Palmitate									15000 IU	15000 IU										
	Beta- Carotene																				
	Retinol Acetate					2500 IU	2500 IU	400 µg	400 µg					1000 µg	1000 µg						
	Mixed Carotenoids																				
	Beta-carotene and vit A																	4500 IU	4500 IU		
B1	Thiamin													2.2 mg	2.2 mg	0.75 mg	0.75 mg				
	Thiamin HCl																				
	Thiamin Mononitrate					0.9 mg	0.9 mg			300 mg	300 mg									0.7 mg	0.7 mg
	Thiamine & thiamine pyrophosphate																	27.5 mg	27.5 mg		
B2	Riboflavin			1 mg	1 mg	1.1 mg	1.1 mg			200 mg	200 mg			2.8 mg	2.8 mg	0.85 mg	0.85 mg			1.1 mg	1.1 mg
	Riboflavin and riboflavin phosphate																	27.5	27.5		
B3	Niacin			15 mg	15 mg	12 mg	12 mg									10 mg	10 mg				
	Nicotinamide													24 mg	24 mg					12 mg	12 mg
	Niacinamide & inositol hexaniacinate																				
	Niacinamide									750 mg	750 mg										
	niacin and niacinamide																	140 mg	140 mg		
B5																5 mg	5 mg			2.7 mg	2.7 mg
	Pantothenic Acid													50 mg	50 mg						
	Calcium Pantothenate			1 mg	1 mg					490 mg	490 mg							70 mg	70 mg		
B6				1 mg	1 mg			1 mg	1 mg					2 mg	2 mg	1 mg	1 mg			1.3 mg	1.3 mg
	pyridoxine HCl					1.1 mg	1.1 mg			350 mg	350 mg	12.5 mg	37.5 mg								
	pyridoxal 5-phosphate																				
	pyridoxine and pyridoxal-5-phosphate																	86 mg	86 mg		
B12	cyanocobalamin			1000 µg	1000 µg	1 µg	1 µg	1.5 µg	1.5 µg	1000 µg	1000 µg			5 µg	5 µg	3 µg	3 µg	175 µg	175 µg	1.5 µg	1.5 µg
Vitamin C	Ascorbic Acid			26.6 mg	26.6 mg			45 mg	45 mg	1500 mg	1500 mg			50 mg	50 mg	40 mg	40 mg	1000 mg	1000 mg	60 mg	60 mg
	Sodium Ascorbate																				
	Calcium Ascorbate																				
	Mixed Mineral Ascorbates																				